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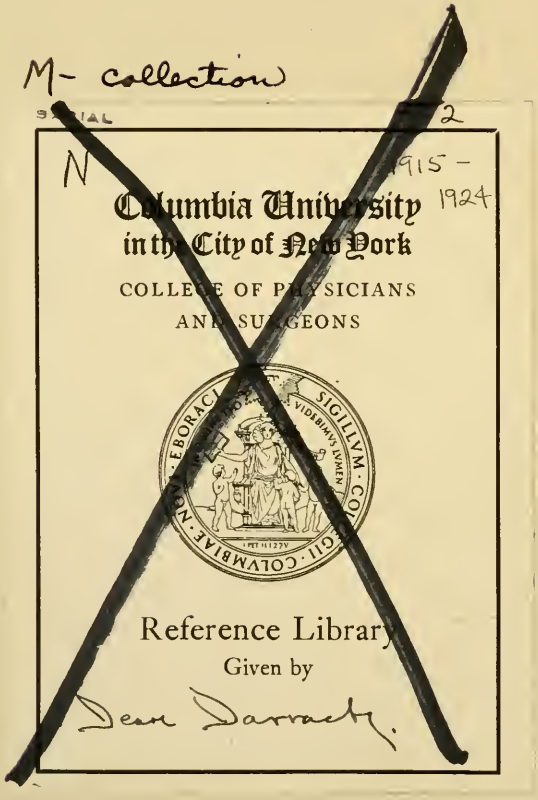

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MEDICAL & SURGICAL REPORT OF THE ROOSEVELT HOSPITAL

New Pavilion for Ward Patients.

Medical and Surgical Report
of
The Roosevelt Hospital
NEW YORK

SECOND SERIES, 1925, BASED ON THE WORK
OF THE YEARS 1915-1924 INCLUSIVE

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PREFACE

When our first Medical and Surgical Report was published, in the year 1915, it was the intention of the hospital staff to get out a new volume every five years. The World War prevented the carrying out of this plan, and now ten years instead of five have passed since our first publication.

The present report contains, as did our first one, articles written by members of the hospital visiting staff expressly for this purpose. The volume contains in addition reprints of papers published in recent years in medical and surgical periodicals by members of our staff.

We wish to thank the publishers of the following journals for their courtesy in loaning us for this purpose the cuts for the illustrations: *The American Journal of Obstetrics and Gynecology; The American Journal of the Medical Sciences; Annals of Surgery; The Archives of Internal Medicine; The Journal of the American Medical Association; The Journal of Metabolic Research; The Medical Record; The New York State Journal of Medicine; Surgery, Gynecology and Obstetrics.*

We also wish to thank Mrs. Pierre Washington Wildey, whose contribution to the hospital has been used in helping to defray the expenses of this publication.

The frontispiece shows the new pavilion for ward patients. It was completed in January, 1924. It is entirely fireproof and was at the time of its completion the last word in hospital construction in this country.

On the main floor is the new *x*-ray plant with complete equipment for diagnosis and treatment. Connected with it is the new cystoscopic operating room.

Alexander T. Martin — Henry C. Thacher
Thomas C. Peightal — Davenport West
Alfred Stillman — Kirby Dwight, *Chairman*

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MEDICAL AND SURGICAL REPORT OF THE ROOSEVELT HOSPITAL NEW YORK

FRACTURES OF THE ELBOW

AS TREATED IN THE OUT-PATIENT DEPARTMENT OF THE ROOSEVELT HOSPITAL*

CONDICT W. CUTLER, JR., M.D., AND
HENRY W. CAVE, M.D.

FRACTURES of the elbow, as considered in the analysis of the cases here presented, are of the lower end of the humerus, and do not include fractures of the upper end of the radius and ulna. Our analysis is based on the study of 64 completed consecutively treated cases. No selection of cases was made. The majority of these fractures occur in children, or young adolescents at a time of life when the reparative processes are most active. In consequence, the eventual result is good as regards union and restoration of function. When injuries of this type occur in adults, as in 4 cases of our series, the return of function is slower and less likely to be perfect, while deformity is more commonly seen.

MECHANISM

The injuries producing these interesting fractures may be briefly summarized as follows:

1. *A Fall on the Outstretched Hand.* In this instance the force is most commonly transmitted through the radius and capitellum to the external condyle, causing a fracture there. A fall on the hand may also occasionally cause a transverse fracture of the humerus by sudden hyperextension, the

* Reprinted from *Surg., Gynec. and Obst.*, May, 1924.

elbow joint being held rigid by the anterior and lateral ligaments. If these ligaments are torn by the sudden hyperextension a dislocation occurs instead of a fracture.

2. *Falls on the Forearm.* When the forearm is flexed at right angles, the force of the blow received on the ulna forces it against the trochlea, and fracture of the internal condyle results. When the forearm is flexed beyond a right angle the force of the fall, transmitted through the ulna, tends to displace the condyles backward. This produces an epiphyseal separation, or the typical supracondylar transverse fracture.

3. *Falls on the Elbow.* The inner condyle may be fractured by direct violence when a fall occurs and the arm is abducted. Similarly the external condyle may be chipped off by a fall with the arm against the body. A fall or blow on the olecranon when the elbow is flexed may produce the rare supracondylar fracture described by Posodas, in which the lower fragment is displaced forward.

4. *Forced Adduction of the Forearm.* This may produce a fracture of the external condyle, or more commonly, of the epicondyle, by transmission of the force through the external lateral ligament.

5. *Forced Abduction of the Forearm.* In this injury, the pull of the internal lateral ligament may fracture the internal condyle or epitrochlea. Occasionally a supracondyle fracture or epiphyseal separation is produced by forced abduction or adduction. When this occurs the condylar fragment is likely to be twisted somewhat in its backward displacement.

Although it has been difficult often to elicit satisfactory histories from our patients as to the exact manner of injury, it will be seen that the various types of fracture observed in our series follow, in a general way, the mechanisms above described.

DIAGNOSIS

Diagnosis of the exact type of fracture occurring at the elbow is often very difficult, because of the marked swelling which appears rapidly after the injury. In supracondylar fractures the lower end of the upper fragment may sometimes be felt projecting forward, if the displacement is great. In epiphyseal separations and in dicondylar fractures this

protrusion is less marked. When the internal or external condyle is fractured the local cardinal signs are more readily elicited because of the relatively superficial position of the parts. The *x*-ray, of course, confirms the correctness of a diagnosis.

TREATMENT

Ashhurst's comprehensive monograph on fractures of the elbow, published in 1910, has done much to popularize the treatment of these injuries by the flexion method. We believe, as the result of observation as well as from the evidence of published reports, that the best results are to be obtained by following a program of accurate reduction, support in hyperflexion, and early mobilization.

Reduction of the fragments to their normal position should be secured if subsequent deformity is to be avoided. This reduction in supracondylar fractures especially, is also necessary to relieve pressure on nerves and blood-vessels. It should be performed at the earliest possible moment.

Our method of reduction does not differ from that usually carried out. When the displacement of the lower fragment is backward, the forearm is grasped and moderate hyperextension is made, the object being to free the fragments. Countertraction is made by pulling backward on the upper arm, while at the same time firm pressure is exerted on the lower fragment to push it forward into position. This being done, the arm is extended, and the forearm abducted to make sure that no loss of carrying angle persists and that the reduction is satisfactory. The forearm is then brought into hyperflexion, abduction being maintained throughout the manipulation.

Every effort was made, in practically all cases of our series, to produce and maintain hyperflexion after reduction. The advantages of this position, we feel, are as follows:

1. By this position the tendency of the forearm, when extended, to press backward the distal fragment is done away with.

2. The tendinous expansion of the triceps is put on tension and acts as a firm splint or sling in holding the reduced fragments in place.

3. In fractures above the condyles the periosteum is stripped up above the line of fracture. If not restored to its normal position by hyperflexion, this may lead to callus formation which will subsequently embarrass function.

4. A certain amount of stiffness is bound to follow these fractures, because of injury to soft parts and extravasation of blood and effusion in the joint. If, at the start, flexion is assured, the more useful functions of the arm are maintained. Subsequent mobilization in the range of extension is more easy and is aided by the force of gravity and the relatively strong pull of the triceps.

When the fracture is through the condyles, manipulation and flexion of the forearm and immobilization are in many cases all that is necessary. However, not infrequently it is necessary to resort to nails driven through the condyle to be sure of a good reduction. Many cases of internal condylar fracture come to open reduction, especially when the internal condyle has slipped into the joint. In our series no case of fracture of the internal condyle was treated by operation, but all were treated by hyperflexion.

Epiphyseal separations are at present coming more to immediate operation. Small incisions are made on either side of the elbow and bone hooks are inserted on either side of the fragment which is pulled forward into position. We believe that these separations, if seen early, will, in the majority of cases, respond satisfactorily to careful manipulation and immobilization in hyperflexion. A slight deformity and moderate loss of function is often better than a complete ankylosis such as occasionally follows infection of the joint brought about by open operation.

The method of treatment by flexion, employed in humerus injuries here reported, was used as follows:

The injured arm was placed in a position of flexion at the elbow as complete as the swelling would permit and in full supination. It was retained in this position by two adhesive straps passing from the upper humeral region to the wrist, one on the outer and one on the inner side of the arm. This dressing was reinforced and the arm supported by a figure-of-eight bandage passing over the shoulder on the injured side, about the elbow and under the opposite axilla.

This dressing was usually inspected after twenty-four hours and the flexion increased if possible. Increase of the amount of flexion was made at twenty-four or forty-eight hour intervals thereafter until the flexion was complete; that is, until the fingers could be made to touch the acromion on the injured side. This result was attained, on the average, about the fourteenth day.

Passive motion was then usually begun, the arm being carried in a sling, and the patient directed to flex the arm completely a number of times a day to preserve the motion gained. Baking, massage and passive motion by the masseuse were customarily begun at this time, and efforts to gain a greater range of extension were instituted. The arm was allowed to hang out of the sling for an increasing length of time each day, and by the third week the patients were instructed to carry weights to increase extension by gravity. If at any time during this procedure the ability to flex the arm completely was lost (as it was in a few instances where satisfactory co-operation of the patients was not obtained) the arm was returned to the flexion dressing and the process repeated.

By this method it was possible to attain a fairly wide range of motion by the time that firm union had occurred, and the more useful motions of the arm, in the range of flexion, were secured early.

REPORT OF CASES

Supracondylar fractures were the most common injuries in this series of 64 complete cases. There were, in all, 32 of these fractures. Nine occurred in the right arm and 19 in the left, while 4 were not recorded. These injuries all occurred in children, the average age of the patients being eight years. The oldest was fifteen and the youngest three.

The nature of the injury was given as "fall on the elbow" in 14 cases, "fall on the outstretched hand" in 6 cases, "fall on the bent arm" in 1 case, while in the remaining 11 the mechanism was not known.

Displacement of the fragment sufficient to require reduction under a general anesthesia was present in 9 cases,

while 1 case required two attempts to attain a satisfactory position. In 5 of the cases reduced the displacement of the distal fragment was reported as backward, while 1 case presented a distinct comminution as well. Twenty-four cases were immobilized in acute flexion, 1 (the comminuted case) in acute flexion in plaster, 4 with right-angle splints, 1 with a split plaster dressing followed by flexion on the ninth day, and 3 by means of extension.

The average duration of passive motion, baking and massage in these cases of supracondylar fracture was thirty and one-half days, while the average duration of treatment was fifty and one-half days. Twenty cases of this group of supracondylar injuries were discharged with good union and full function, while 12 were not cured at the time of stopping treatment. Of these latter 8 subsequently reported with perfect results, while 4 were not cured when seen at the follow-up. Of the 4 cases not cured, 2 had a diminution of the normal carrying angle, but with complete restoration of flexion and extension; 1 (the case mentioned as having a bad comminution) had no deformity, but showed a limitation in motion 5 degrees short of full extension. Flexion was complete. In the fourth case, at the time of reduction, a plaster-of-Paris right-angle splint was used by the family doctor. The carrying angle was perfect, but the patient lacked full extension by 10 degrees. Flexion, however, was complete.

Four *internal condyle fractures* were recorded. One occurred in the oldest patient in the series, a woman of sixty. As nearly as could be ascertained she had fallen with the arm adducted and extended beneath the body. Deformity (gun-stock) was present, and abnormal mobility and crepitus. *X*-ray examination revealed the internal condyle displaced forward. Reduction under anesthesia was done, followed by immobilization in flexion. Motion was begun on the seventeenth day and continued for eighty-three days with massage and baking. The patient was discharged on the one-hundredth day with good union, no deformity, but with range of motion limited (mid-flexion to mid-extension). On recall, fifteen months later, flexion was complete, extension beyond 130 degrees, and the arm was reported "stronger and useful."

Of the other 3, 1 was caused by direct blow, the other 2 by indirect violence. All were treated by acute flexion. The average number of days before the beginning of motion was eleven and eight tenths, and the average number of days under treatment was thirty-eight and three tenths. A cure resulted in all cases.

There were 7 cases of *external condyle fractures*, 2 right and 5 left. All resulted from "falls on the elbow." Displacement in 1 case was reduced under anesthesia. These cases were put up in hyperflexion. In all the cases of this group the patients were discharged from the hospital with full restoration of function.

Epitrochlear fractures were 7 in number, 3 on the right side, 2 left, and 2 not recorded. Four resulted from "falls on the elbow," 1 from "fall on the arm," and 1 from "catching and twisting the arm in the banisters," while 1 was associated with a backward dislocation of both bones of the forearm. The average age of the patients was eleven and two-tenths years.

All 7 cases were treated by the flexion method. No reductions were needed. Motion was begun on the average on the sixteenth day; average duration, twenty-one days. The cases averaged thirty-eight days of treatment. Four patients were cured before being discharged, while 3 presented limitation of extension at the time treatment was abandoned. These 3 patients subsequently reported complete return of function on recall.

Fractures of the capitellum were 4 in number, 3 being in the right arm, 1 in the left. One injury resulted from a "fall on the extended hand," one from "twist of the arm," and the other 2 from a "fall on the elbow." The patients' ages were nine, twelve, eleven and three years.

Treatment was by acute flexion in each case, there being no reduction required. The average duration of treatment was nineteen days. Three patients were discharged cured, while one abandoned treatment at the end of twenty-four days, at which time full flexion to right-angle flexion was the range of active motion.

This patient, a boy of twelve, had suffered an injury of the elbow four years before the fracture for which he was

under care. Since that time he had had a diminished carrying angle. When seen eight months after leaving our care, the loss of carrying angle was still present, but the range of motion had increased at the elbow joint. His final result was recorded as "full flexion, practically complete extension." There was little disturbance of function.

This group included 2 cases of *intercondylar fractures*. In 1 of these the injury was caused by "a fall on the tip of the elbow," while in the other the injury was sustained by the arm being caught and twisted in a machine belt. One of these fractures was in the right arm, one in the left. The ages of the patients were eleven and thirty years.

Treatment in one case was by the acute flexion method. The adult case required reduction and the application of plaster, followed by the acute flexion treatment. The average time to the beginning of passive motion was eight days, to baking and massage sixteen days, while the average duration of these procedures was fifty-two days. The average length of treatment was seventy days. The results obtained in this group were as follows: Discharged cured, 1; abandoned treatment, not cured, 1 (adult). The latter still had limitation of extension at the expiration of five years.

One case of *external epicondyle fracture* was seen. This injury resulted from "a fall on the elbow." The patient was eight years old. No reduction was necessary, the treatment being by the acute flexion method. Motion was begun on the eleventh day, the total duration of treatment being twenty days. Patient was discharged with good union and complete function.

Our group of *epiphyseal separations* consisted of 7 cases, 3 right and 4 left, all treated by hyperflexion following reduction. The average number of days before the beginning of motion was eighteen, and the average number of days of passive motion and massage was twenty-three. The average number of days under treatment was forty-six and six-tenths. All cases secured excellent results.

RESULTS

Number of cases, 64. Cured, 76.5 per cent. Results at time of discharge: Not cured, 25 per cent; cured, 68.7 per cent.

Late results on cases not cured at time of discharge: Not cured, 31.2 per cent. Cases ultimately cured (complete flexion, complete extension, full supination and pronation), 89 per cent.

There were 5 cases without complete flexion or extension, incomplete pronation or supination, or gunstock deformity.

TECHNIQUE OF PARTIAL COLECTOMY BY THE MIKULICZ TWO-STAGE METHOD*

CHARLES N. DOWD, M.D.

IN the *Annals of Surgery* for February, 1920, the writer published an article on "The Advantages of the Mikulicz Two-stage Operation of Partial Colectomy." The references to this article have been mainly of two varieties: one, communications from a number of experienced surgeons acknowledging the advantages of the principle of "exteriorizing" the growth before the intestine is opened; the other, requests for information about various details of operative technique.

There have been so many inquiries of the latter type that it seems advisable to publish a further description of this technique by giving the details of a single illustrative case of partial colectomy for cancer at the sigmoid. This is done in the hope of further popularizing an operation which diminishes the dangers of patients with cancers of the large intestine between the hepatic flexure and the lower sigmoid, or with other lesions which call for partial colectomy in this region.

In the previous article, 8 cases of partial colectomy were reported, with 1 death. Since that time the writer has successfully operated upon 3 additional cases: 1 for cancer of the transverse colon, 1 for Hirschsprung's disease, and 1 for cancer of the sigmoid. This low mortality rate in a short series of cases indicates the comparative safety of the procedure, but it should not mislead the reader. Individual operators continually have short series of cases which give better results than can be maintained in long series.

HISTORY OF PATIENT

Female, married, a rather thin woman, aged thirty-two years, came to The Roosevelt Hospital March 13, 1920, suffering from long-continued intestinal obstruction.

* Reprinted from *Ann. Surg.*, Dec., 1920.

She stated that she had been in excellent health until two months previous, when she had cramp-like pains across the abdomen, especially in the lower left side. These were severe and were accompanied by constipation. She went for two weeks with very slight fecal passage. Large quantities of feces then passed and she was relieved. For more than two weeks she then had suitable bowel movements.

FIG. 1. Primary incision. Used for exploration, mobilization of intestine and for removal or mobilization of enlarged lymphatics.

On admission she stated that the last bowel movement had occurred twenty-six days ago. During that time she had eaten very little, but had taken various forms of broth. She had suffered much from abdominal pain, but had vomited very little, excepting after taking castor-oil. Occasionally the return from the enemas had been blood-tinged. Just before coming to the hospital severe vomiting had begun and hence she sought immediate relief. She was in reasonably good general condition. Heart and lungs sound; abdomen dis-

tended; visible peristalsis; no tumor palpable either by examination or by rectum.

DESCRIPTION OF OPERATION

The details of the operation for this patient are shown in the accompanying plates. They give a fair indication of the average procedure.

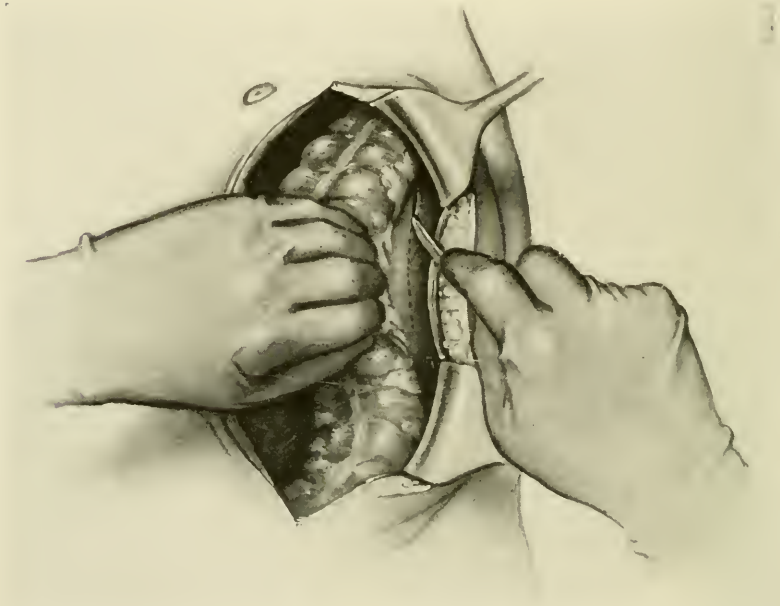

FIG. 2. Incision of outer leaf of peritoneum beside descending colon so as to secure suitable mobility of that part of colon.

1. *Primary Incision.* A low, 5- or 6- inch incision near the median line gives opportunity for suitably exploring the abdomen, learning the site and character of the primary lesion, and searching for metastases and lymphatic enlargement. With or without enlargement, it also permits the mobilization of the growth in operable cases. Figures 2, 3, and 4 indicate the portion of work done through this incision in this case.

2. *The incision of the outer leaf of the peritoneum of the descending colon,* as advocated by Moynihan and others and

as indicated in Figure 2, is easily accomplished and secures wonderful mobility of the corresponding portion of the intestine. When carried upward sufficiently, it permits the mobilization of the splenic flexure.

3. *Removal of Lymphatics.* It is desirable to examine the lymphatic areas which are liable to infection. Jamieson and

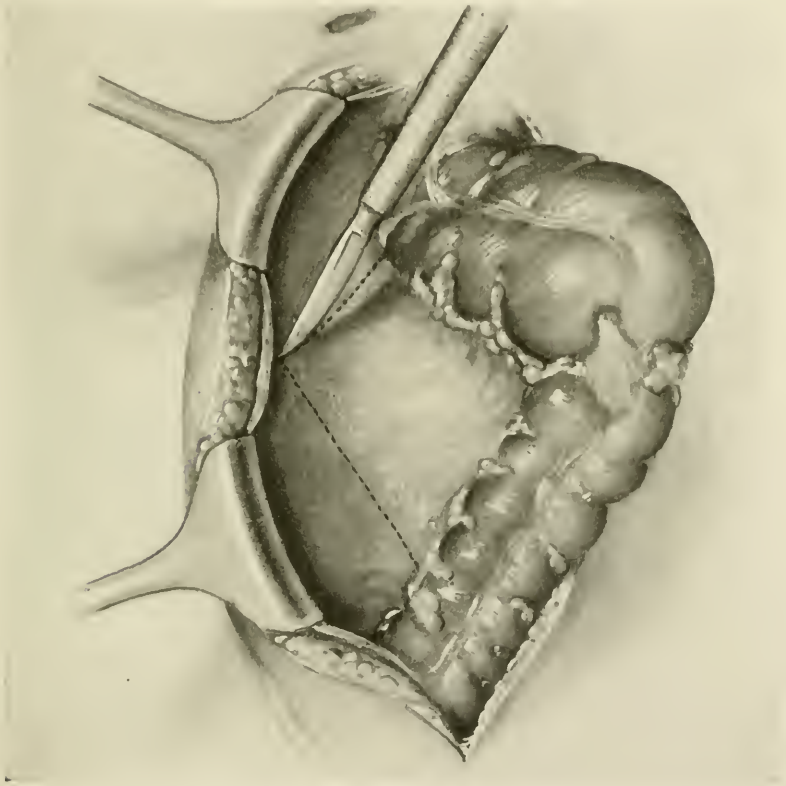

FIG. 3. Exposure and removal or mobilization of enlarged lymphatics and part of mesosigmoid.

Dobson* have carefully investigated thean atomy of these areas. It is not always practicable to remove them completely, nor is it always necessary. Numerous observers have shown that cancer of the colon may long remain a local disease.

* *Proc. Roy. Soc. Med.*, 1908–1909, Surgical Section, p. 149.

Clogg* made post-mortem examinations in 18 patients with cancer of the pelvic colon. Enlarged lymph-nodes were noted in 17 instances, but only in 6 were they at a distance from the colon. He found that, in one-third of the cases examined, enlarged lymph-nodes did not show cancer cells. The judg-

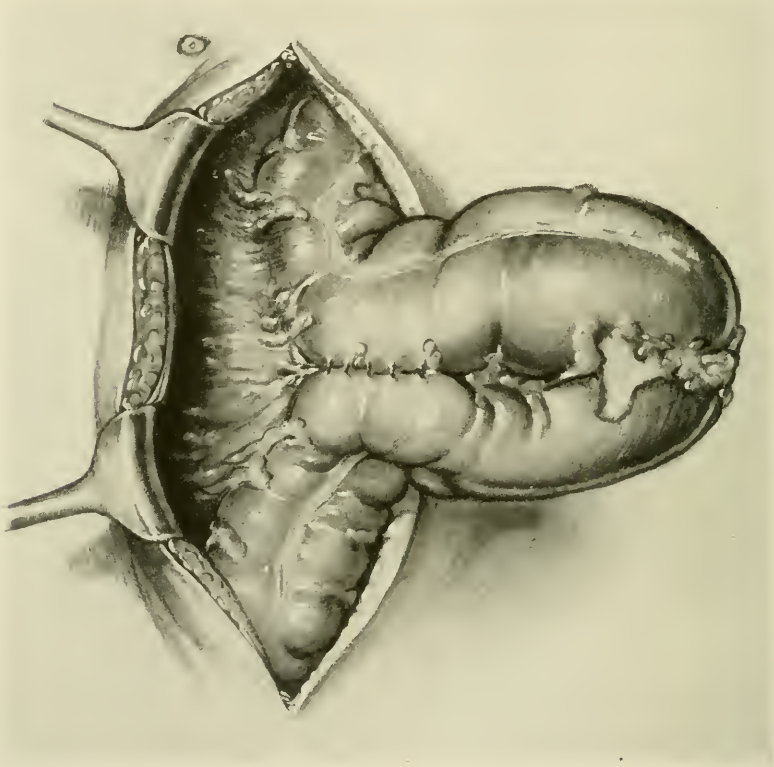

Fig. 4. Stitching of afferent and efferent legs of intestine so as to form a septum which is suitable for later clamping.

ment of the individual surgeon must determine the extent of the lymphatic area to be removed.

In this instance the small intestines were retracted to the right and the mesocolon was exposed as far as the spine, the peritoneum was incised, and the lymph-nodes were mobilized

* Clogg, H. S. Cancer of the colon. *Lancet*, 1908, *ii*, 1007.

and either removed at once or pushed toward the sigmoid. Branches of the left colic and inferior mesenteric arteries were clamped, tied and cut, but the main trunks of both of these arteries were preserved. A sector of the peritoneum, with apex at inferior mesenteric artery and base at the sigmoid, together with the adjacent lymphatics, was mobilized and pushed to the sigmoid. The breadth of this sector must vary somewhat with the individual case. Since the lymphatics extend along the intestinal wall to the next afferent arterial branch, it is desirable to remove a corresponding portion of the intestine, with its adjacent arterial loops, and the incision in the mesosigmoid should be large enough to permit this.

The real point at issue is that in the two-stage operation the extent of lymphatic dissection and the length of the removed portion of intestine may be as great as in the one-stage anastomosis. Tension is to be avoided in any instance, but the danger of moderate tension is not so great in the two-stage procedure as in the one-stage procedure. Unless the abdominal wall is unusually thick, patients who give suitable facilities for one-stage anastomosis are likely to give equally good opportunity for two-stage procedure.

4. *Stitching of Afferent and Efferent Legs of Intestine so as to Secure a Good "Spur."* Sound portions of the afferent and efferent legs of intestine were selected at safe distance from the cancer and stitched together with fine catgut for a distance of 2 in. or more. This secured suitable apposition between these portions of intestine. A good septum was thus formed to which a clamp was safely applied at a later time.

5. *Exteriorization of Cancerous Portion of Colon.* This is best accomplished through a small separate incision at a convenient site. In this instance finger pressure was made from within the abdomen a little above and internal to the anterior superior spine of the ilium, and a small intramuscular incision of the McBurney type was made there. The diseased loop of intestine was then drawn through this incision. In this instance there was so much gas pressure from above that the extruded intestine "ballooned up" like an inflated rubber bag. The edges of the skin were stitched to the intestinal wall.

FIG. 5. Primary wound closed. Diseased intestine delivered through small secondary intramuscular wound. (In this instance it was distended by pressure of gas from above.)

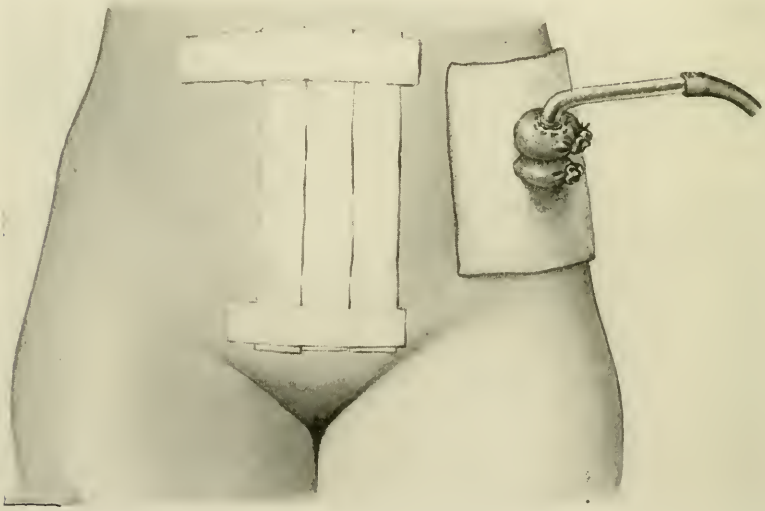

FIG. 6. Primary wound covered by aseptic dressing. Secondary wound smeared with ointment and protected by gauze. Protruding parts of afferent and efferent intestine ligated. Diseased portion of intestine ablated. Paul's tube inserted in protruding part of afferent intestine so as to secure and temporarily control drainage.

The primary incision was then closed in layers and covered with a small, sterile-gauze dressing. This in turn was completely covered in with strips of adhesive plaster which extended over to the surrounding skin. In this way healing of the primary wound by first intention was secured.

The small size of the new incision and the undisturbed condition of the tissues about it leave little likelihood of mural abscess about the stoma.

6. Treatment of Excluded Portion of Colon. After the skin and adjacent portion of colon have been well smeared with a 10 per cent boric acid ointment, gauze is laid about them.

We now have the abdomen shut off. Since the intestine has not been opened, there has been little likelihood of infection. In Mikulicz' early cases the loop of cancerous intestine was permitted to slough in the dressing. This, however, was not done in his later cases and is unnecessary. A ligature can be placed about each loop of intestine outside the gauze dressing. The cancerous loop of gut can be ablated. The time for opening the protruding intestine depends upon the condition of the patient. In some instances it may be deferred for forty-eight or even seventy-two hours. In this instance, owing to the pressure of gas from above, an immediate opening was desirable, therefore a purse-string was placed in the upper leg of intestine between the ligature and the gauze dressing, a Paul's tube was inserted and held fast by a tightening of the purse-string. This permitted gas and feces to escape without soiling the dressing. The purse-string joint held for

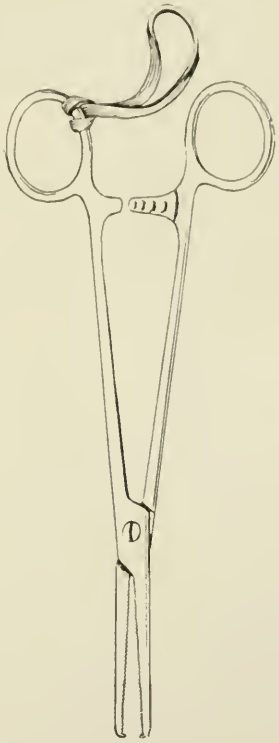

FIG. 7. Clamp for dividing the "spur" by pressure At first the pressure was secured by a rubber band applied to the handles; afterward the ratchet is used for progressive tightening of the clamp.

twenty-four hours, which was sufficient to permit a reasonably good union between the abdominal wall and the intestine, and thus prevent infection at that point.

7 and 8. *Clamping of the Spur.* The ligatures about the ends of the intestine were removed after forty-eight hours. A "double-barrelled" intestinal stoma was thus established which provided an exit for the intestinal contents. After nine days the union of the abdominal wall was firm. There

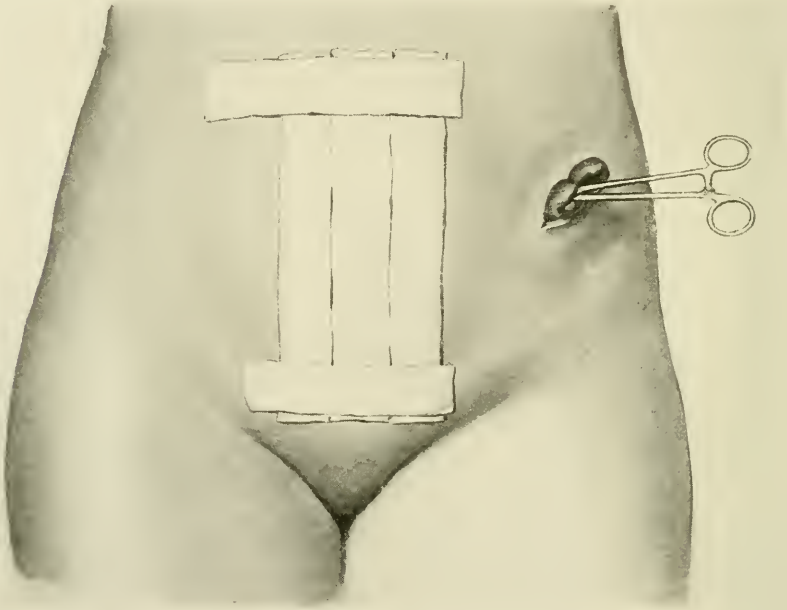

Fig. 8. Clamp applied to septum.

was no evidence of surrounding inflammation there and the crushing of the spur between the two legs of intestine was begun. Various clamps have been used for this purpose. The one which bears the name of Mikulicz is believed to be a very efficient one. We have tried various forms of clamps and, at the present time, use an ordinary Kocher clamp (Fig. 7), or a similar clamp without teeth at its end. After inserting fingers on each side of the septum so as to determine the relationship of the parts, the clamp is applied and an elastic band applied about the handle so as to make firm

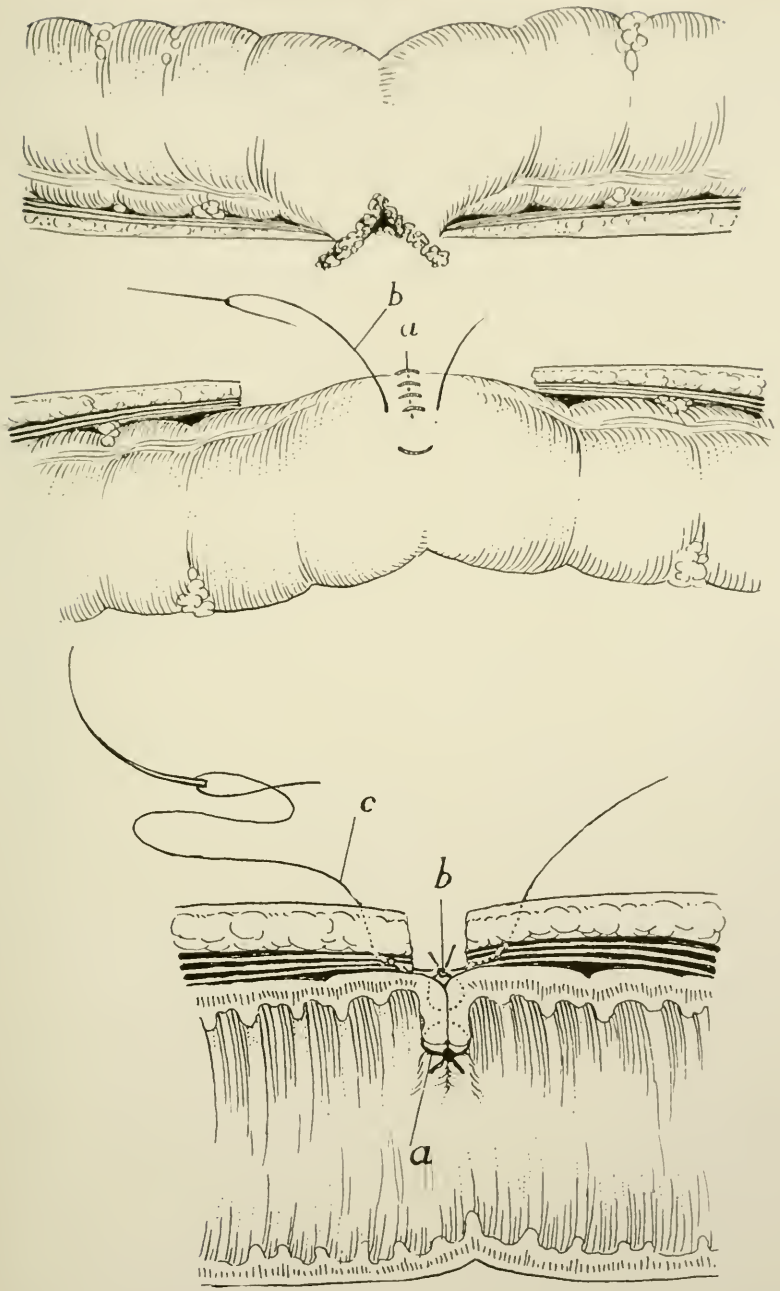

FIG. 9. Closure of stoma. The intestine is separated from its attachment to the abdominal wall so as to expose its peritoneal surface. The lower leg is then pulled upward and the upper leg downward. Interrupted chromicized gut stitches (*a*) are taken through the entire intestinal wall at the upper and lower edges of the stoma and tied with their knots inside the intestinal lumen. This row is then reinforced by Lembert stitches (*b*). The edges of the abdominal wall are then approximated by silkworm-gut stitches (*c*), leaving provision for possible leakage.

pressure. At the end of one or two days the first notch of the ratchet was fastened. On successive days, additional pressure was applied (Fig. 8) and the clamp came away on the fifth day. In this instance the artificial anus discharged intestinal contents regularly and the mouth of the stoma contracted moderately.

9. *Closure of Stoma.* On the twenty-fifth day an effort was made to close the stoma. The skin was dissected away from the margin of the intestine. The upper leg was pulled downward from above (Fig. 9) and the lower leg was pulled upward from below, thus securing enough intestine for good serous apposition of the ends. The peritoneum was slightly opened for this procedure, and the edges of the peritoneal opening were easily secured by a few catgut stitches. The first row of stitches was then taken between the intestinal ends. They were interrupted chromic gut, included the entire intestinal wall, and the knots were tied inside the lumen. A second row of Lembert stitches of chromic gut was then taken to secure apposition outside of the first row. The edges of the abdominal wound were then drawn together with silkworm gut, leaving a very small opening for the escape of leakage. In this instance the closure was not complete and after two weeks a clamp was applied to a portion of the spur which remained. After this clamp came away the stoma was again closed by two rows of stitches and the suture line was supported by loose, silkworm gut stitching through the overlying abdominal wall. The wound then closed satisfactorily and the patient left the hospital on May 26th. The period of her operation and after-treatment was, therefore, ten and five-sevenths weeks. This was longer than a successful one-stage operation would have taken. A one-stage operation, however, was not to be considered for this case. The intestine was too greatly distended and contained too much foul fecal material. A preliminary colostomy and later one-stage operation would probably have taken longer and would have been much more dangerous.

THE ADVANTAGES OF THE MIKULICZ TWO-STAGE OPERATION OF PARTIAL COLECTOMY*

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THE early intestinal resections were largely done by the help of temporary artificial ani. As surgery progressed the elements which control sepsis were better understood and the wonderful healing power of the intestine was better appreciated. Immediate suture was successfully practiced and the one-stage operation became the procedure of choice either with immediate closure of the wound or with provision for drainage. An immediate healing with prompt restoration of function is surely more desirable than a delayed union and the discomforts of even a temporary intestinal stoma.

There are, however, certain advantages inherent in the two-stage operation. In 1902 Mikulicz formulated these advantages, described the operation which ordinarily bears his name and recorded cases which showed remarkable reduction in mortality rate. He had then used the procedure for more than five years. He thoroughly mobilized the portion of intestine which was to be removed and delivered it through the abdominal wound after stitching together the serous surfaces of its afferent and efferent portions. He then closed the incision to the emergence of the intestine, stitched the skin edges to the intestinal wall and applied protective ointment and a surgical dressing over the incision. This was all accomplished without opening the intestine. He either left the extruded portion in the dressing to be removed at a later time or excised it at once and provided for drainage at a safe distance from the wound. A temporary stoma was left. The "spur" was clamped through at a later time and then the intestinal ends brought together by suture.

Many surgeons have adopted this operation on account of its diminished mortality rate. However, the records published in surgical literature indicate that it is used only in a moder-

*Reprinted from *Ann. Surg.*, Feb., 1920.

ate portion of those cases for which it might be considered suitable. For instance, in the last ten volumes of the *Annals of Surgery* we find records of 26 operations for obstructive disease of the colon. They were distributed as follows:

End-to-end suture	9
Lateral anastomosis	7
Short-circuiting	6
Mikuliez operation	2
Exploratory operation	1
Colostomy	1

If we study the 32 cases of cancer of the splenic flexure which Hartwell collected from the literature from 1906 to 1918, we find the following records:

Mikuliez, or similar procedure	9
Lateral anastomosis	7
End-to-end suture	5
Short-circuiting	3
Colostomy	6
Colostomy with extirpation of tumor	1
End-to-side anastomosis	1
Inoperable cases	6

These reports show great diversity of method and suggest the desirability of further consideration of certain elements which bear on the relative advantages of one-stage operations and two-stage operations when portions of the intestine are to be removed. These elements are:

1. Septic intestinal content.
2. Extent of peritoneal intestinal covering.
3. Condition of patient.
4. Peritoneal sepsis.
5. Conservation of nutrition.
6. Skin irritation from leakage of intestinal content.
7. Reflex effect of fastening different parts of the intestine to the abdominal wall.

These elements differ in different parts of the intestine and in different patients.

Small Intestine. The small intestine presents elements which favor one-stage operation in almost all instances. The intestinal content is fluid and, ordinarily, is rapidly moving and has little septic power. The peritoneal covering

is close to the muscular wall of the intestine excepting at the small mesenteric border, and hence gives abundant opportunity for strong opposition. Cancer is rare here and hence we do not often have to deal with debilitated patients. Furthermore, the disadvantages of the two-stage operation apply to the small intestine with especial force. Inanition results from too much intestinal leakage. Skin irritation, or even skin digestion, follows the leakage of fluid which still has digestive power. The reflex disturbance from fixation is greater from the small than from the large intestine. Hence the two-stage operation is applicable to the small intestine only in especial emergencies. For instance, strangulated hernia with gangrene of the intestine and spreading infection of the adjacent tissues.

Ileocecal Region. At the ileocecal region the conditions still favor the one-stage operation. The intestinal content is still fluid, it has only moderate infective power and ordinarily moves with fair rapidity. The peritoneum of the ileum is close to the muscular coat excepting at the mesenteric border, and the peritoneum of the large intestine gives abundant opportunity for serous apposition of either lateral or end-to-side anastomosis. Provision for possible leakage is easily obtained.

Colon. Hepatic Flexure to Terminal Sigmoid. The colon from the hepatic flexure to the terminal sigmoid is the region for which the two-stage operation is especially considered. This region furnishes nearly 70 per cent of the intestinal cancers above the rectum.[1] Here we have an intestinal content which is semi-solid, or possibly solid. It holds vast numbers of bacteria. Mayo states that it has been shown that one-quarter to one-third of the stool bulk is due to bacterial growth. Partial obstruction exists in a large proportion of the cancers of this region which come to operation, hence this septic intestinal content cannot be satisfactorily eliminated and forms a serious menace to satisfactory healing.

The peritoneal covering is frequently defective. This defect in the upper part of the descending colon is due to the anatomical arrangement which usually leaves the posterior portion of the gut uncovered by peritoneum. However, the deposit of fat between the peritoneum and the muscular

coats of the intestine is sometimes the main barrier to satisfactory serous apposition. In the sigmoid and descending colon one frequently notices at operation that the strip of peritoneum which lies close to the muscular wall is only one-half to three-quarters of an inch in width and that there is a thick deposit of fat elsewhere. This fat deposit is shown in the appendices epiploicae, but in many instances is massive and really envelops a large part of the intestinal wall. Of course, in those patients who are debilitated by cancer it has usually been absorbed, but some patients come to operation in whom it is still present; hence operation must be planned with the understanding that fat deposit may hamper serous apposition of the divided intestinal ends.

The condition of the patient may be a strong barrier to a successful one-stage operation. The majority of these patients suffer from cancer and have suffered for a long time before they come to operation. They have little resisting power and hence operative procedure must be planned so that they will not have more than they can endure.

Peritoneal sepsis does not often occur in these patients, but a perforation is occasionally found which leads to considerable peritoneal sepsis and hence forbids a type of anastomosis which otherwise might be made.

The interference with nutrition, the skin irritation and the reflex effect of fastening the intestine to the abdominal wall are all minimized in the two-stage operation on the colon as compared with the small intestine.

We therefore have many reasons why a two-stage operation should be used in a large number of partial colectomies.

Statistics Comparing Results of Different Types of Operation. If we study records of operations we find further reason for using the two-stage procedure. Mikulicz[2] emphasized the advantages of this procedure and gave detailed reports of its efficiency in the Breslau clinic. The mortality of intestinal resections by the one-stage operation was 42.9 per cent, whereas by his two-stage operation he did 16 cases with only two deaths—a mortality of 12½ per cent—and these two deaths were not, primarily, due to the operation.

The procedure has been much used in the intervening years. Oppel[3] quotes Finkelstein as showing in the collective

study of results that the mortality of the one-stage operation had been 29 per cent, and that of the Mikulicz two-stage operation had been 16 per cent.

Mayo[4] states that the adoption of the Mikulicz-Bruns method has probably done more to extend operability and reduce mortality in resections in the second half of the colon than any other factor. By adopting this method in a large proportion of the operations he resected the left half of the colon, including the splenic flexure but not including the rectum, 184 times, with a mortality rate of 17 per cent.

Hartwell's[5] recent study of cancer of the splenic flexure is very important, although discouraging. After a careful study of the literature, he estimates that the probable operative mortality of all cases, up to the present time, is over 60 per cent. But the results from operation in many stages is much better than that in one stage. He states that his "collected cases show a mortality approximately three times greater in the one-stage than in the many-stage procedure. Careful study indicates that the failures in the one-stage operation would have been avoided by the other mode of attack. These failures arose almost entirely from leakage somewhere along a suture line, with a resultant peritonitis or improperly drained abscess."

The late James P. Tuttle once told me that he had successfully done five successive partial colectomies by the Mikulicz method, whereas his previous mortality rate, in similar conditions by other methods, had been 33 per cent.

We thus see that there are abundant records to show that the two-stage or many-stage operation has a much lower mortality rate than the one-stage operation.

Record of Personal Operations. The author's early cases were mostly admitted to the hospital on account of symptoms of obstruction. It was not always possible to secure satisfactory cleansing of the intestine. Anastomosis with immediate return of the intestine to the abdomen was sometimes successful and satisfactory, but, even in those patients in whom a preliminary colostomy was done, there were enough failures to lead to a search for a better method. The following cases illustrate the use of the Mikulicz method. The mortality rate, one in eight, is much better than that obtained by immediate suture.

Case I. *Adenocarcinoma of Sigmoid.* Male, aged fifty-one years. Roosevelt Hospital, No. A15023. Operation March 29, 1919. Fourteen months previously he had had an abscess beside the descending colon which had healed but had again been opened in February, 1919. At operation, an adenocarcinoma was found in the upper part of the sigmoid. This was mobilized and the diseased part of the intestine was delivered through the abdominal incision. The procedure was much hampered by the presence of the discharging sinus. A loop of small intestine was adherent to the sigmoid and was necessarily exposed to the infection from this sinus. It was, however, returned to the abdominal cavity. The diseased portion of the colon was delivered through the abdominal wound. Wound closed to the point of emergence after the afferent and efferent legs of intestine had been united. The wound was protected by ointment and gauze, protruding portions of intestine double ligated at a distance from the skin edges, tumor excised outside of primary dressing. Exposed mucous membrane cauterized. Ligatures cut forty-eight hours later. The patient died of general peritonitis six days later. His death was apparently due to infection from the sinus and attached coil of small intestine which had come in contact with it.

Case II. *Adenocarcinoma of Descending Colon.* Female, aged sixty-five years. One-year intermittent pain in left side. Worse of late. Had lost 25 lbs. in weight. Palpable mass in left side of abdomen. Operation June 29, 1918. Intermuscular incision above and in front of anterior superior spine of ilium. Descending colon mobilized and delivered through the wound. Annular growth just above the sigmoid. Serous surfaces of afferent and efferent portions united with catgut. Wound closed to the emergence of intestine. Intestine stitched to skin; also further secured by tape. Ointment and surgical dressing applied over the wound. Protruding intestine double ligated. Diseased portion ablated external to the ligatures. Mucous membrane cauterized and secondary dressing applied. Ligatures removed on second day. Spur clamped in two weeks.

Second operation July 30, 1918. The operation was done in an adjoining city and patient had not been seen by the author since the primary operation. A clamp was applied to that portion of the spur which still remained. The intestinal edges stitched together to the emergence of this clamp and the union was reinforced by stitches through the fascia and skin. The wound closed promptly excepting for a very small sinus. The sinus soon closed completely. She made an excellent recovery and is now in good health with no evidence of recurrence.

Case III. *Adenocarcinoma of Transverse Colon.* Male, aged fifty-three years. Roosevelt Hospital, No. A14317. Eleven months' history of cramp-like pains intermitting and recurring. Loss of weight, 15 lbs. April 15, 1918, partial colectomy through an incision in upper right rectus. Gastrocolic omentum separated from greater curvature of stomach. Growth mobilized and delivered; serous surfaces of afferent and efferent legs united with catgut. Wound closed to emergence of intestine. Skin stitched to intestinal wall. Dressing applied to abdominal wound. Clamps applied to intestine leaving about 1½ in. between clamps and abdominal wound. Clamps removed in thirty-six hours. There was satisfactory healing, but the patient was much

debilitated and did not gain strength rapidly. Clamp applied to spur on May 3d. Attempt to close stoma by loosening the attachments and applying stitches in layers on May 18th. This was only partially successful and was repeated on June 24th. After this there was slight leakage, but the wound was entirely closed on September 3d, and the patient has remained in excellent health ever since. Has done routine duty as policeman, and is now in excellent health.

Case IV. *Adenocarcinoma of Descending Colon.* Female, aged fifty-two years. Roosevelt Hospital, No. A14356. Abdominal pain, colic, vomiting recurring in intermittent attacks six weeks or more. Operation May 11, 1918. Long incision through the left rectus muscle. An annular constricting adenocarcinoma was found in the descending colon just below the level of the costal border. This and the adjoining portion of the intestine were mobilized and delivered through a second, left intermuscular incision. Serous surfaces of afferent and efferent legs united with catgut. Wound closed to the emergence of intestine. Skin edges stitched to intestinal walls. Intestine further held by glass rod. Wound dressed with ointment and gauze. Intestine double ligated outside the layers of gauze. Tumor and adjoining intestine ablated. Mucous membrane cauterized. Further dressing applied. Two days later the constricting ligature was removed from the afferent intestine; satisfactory intestinal stoma established. Spur clamped in two weeks. Colostomy opening closed in layers July 22d. Patient left hospital September 12th. All steps in her procedure were slow on account of her weakened condition. Wound closed satisfactorily, and she remains in excellent health at the present time.

Case V. *Colloid Carcinoma of Descending Colon.* Female, aged thirty-two years. Roosevelt Hospital, No. A8521. Four months' history of cramp-like pains in abdomen and back. Operation May 9, 1917. Growth and adjoining portion of descending colon mobilized and brought through left abdominal wound. Serous surfaces of afferent and efferent legs joined with catgut. Wound closed to emergence of intestine. Skin edge stitched to intestine. Intestine further stabilized by glass rod. Two ligatures applied outside the dressing. Intestine excised outside the ligatures. Mucous membrane cauterized. Ligatures removed two and three days after operation. Suitable stoma established. Spur clamped two weeks after operation. Ends of intestine united on June 12th. Patient left hospital, with wound healed, on June 30th.

Case VI. *Adenocarcinoma of Sigmoid.* Female, aged thirty-nine years. Roosevelt Hospital, No. A6340. Operation June 19, 1915, for a recurring cancer of the sigmoid. Intestine mobilized. Afferent and efferent legs united with catgut. Mobilized portion delivered through the left intermuscular incision. Skin edges stitched to intestinal wall. Dressing applied. Intestine double ligated outside the primary dressing. Ligatures about afferent end of intestine removed in forty-eight hours. Stoma established. Spur clamped in about two weeks. Ends of intestine sewed together July 29th. Patient left hospital, with stoma closed, August 15th.

Case VII. *Extensive Tuberculosis of Caput Coli and Lower Ileum.* Male, aged thirty-five years. General Memorial Hospital, December 12, 1912. One-stage operation not done on account of infection which was present. Mikulicz procedure with immediate removal of diseased intestine. Stormy

convalescence owing, in large measure, to illness not connected with the intestine. Spur cut down; stoma closed. Patient left hospital after two months and made excellent recovery after three additional months of treatment, and remains well at the present time.

Case viii. *Diverticulitis. Perforation. Abscess Formation.* Male, aged sixty-four years. Roosevelt Hospital, No. B3281. Three months' intermittent, left abdominal pain and constipation. Large palpable mass in left side of abdomen. Operation September 13, 1912. Large mass, composed of perforated descending colon and encapsulating omental and pericolonic fat, mobilized and delivered through left lateral incision. Serous surfaces of afferent and efferent intestine stitched together with catgut. Abdominal incision closed to the emergence of the intestine. Skin edges stitched to intestine and retaining tape placed between the intestinal loops. Dressing applied. Ligation of protruding intestinal loops outside of primary dressing. Ablation of inflammatory mass. Exposed mucous membrane cauterized. External dressing applied. Ligature removed after seventy-two hours and stoma established. Part of spur clamped on fifth day to seventh day. Remaining spur clamped at a later time. On October 13th, an effort was made to close the stoma. This was successful excepting for a small fistula which was closed on November 3d. Patient left hospital on December 14th with wound satisfactorily closed.

This series of cases is too small for extensive deductions, but it is sufficient to indicate that the Mikulicz procedure is far safer in the colon than the one-stage procedure. The low mortality rate—12½ per cent—corresponds to that of other operators. The one fatal case was due to a rare complication; we do not often find an open sinus and a loop of small intestine adherent to the infected area.

Of course, delay in healing, unpleasant convalescence and probability of hernia constitute the main barriers to this procedure. In this series the delay has often been longer than was absolutely necessary. While a debilitated patient is gaining strength steadily, but slowly, one hesitates about even moderate surgery when a little longer waiting is sure to make the closing of the stoma easier. Absence from the city also occasioned delay in some instances. Mayo begins the clamping of the spur ten or twelve days after the primary operation and expects its division to be complete in six more days. "A few days later the resulting colostomy can be closed by a simple extra-peritoneal operation." In two of my cases the healing was complete in respectively six and one-half and nine and one-half weeks. In 5 cases small sinuses remained for three to five months before final healing

occurred. These were not enough to occasion serious inconvenience and the patients preferred delay to further stitching. When we appreciate the greater safety, we may be sure that most patients would be willing to purchase this safety by a delay in convalescence and the associated discomforts.

Final Results. Proper mobilization of the desired portion of the intestines is the first element in obtaining good final results. If the adjacent tissues or lymph-nodes are involved, they, too, are to be removed when possible. This is done without regard to the method of excision. Considering the increased percentage of recoveries, the final results of the two-stage operation are much better than those of the one-stage operation.

Applicability of the One-stage Procedure. Without doubt, there are patients in whom the one-stage operation can be successfully done. Such patients should be fairly strong and their colons should be nearly empty and should be comparatively free from fat. Before deciding to use this method, one may well remember the brilliant results which Mayo and Mikulicz have obtained by the two-stage procedure, and Hartwell's studies, which show that the one-stage procedure has had a mortality rate three times greater than the many-stage method.

It is not my purpose to advocate the two-stage procedure for all cases, but rather to call attention to its advantages and to urge its use in the average case as it now comes to us in the hospital, reserving immediate suture in the colon for those patients who are especially fitted for it.

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THE RELATIONSHIP BETWEEN CERTAIN FORMS OF INTESTINAL OBSTRUCTION, CHRONIC PERITONITIS AND CHRONIC MULTIPLE SEROSITIS*

Charles N. Dowd, M.D.

IN 1908, before the Surgical Section of the American Medical Association, Dr. Miles F. Porter[1] of Fort Wayne, Ind. and Dr. William H. Welch of Johns Hopkins University presented a remarkable specimen of an intestine which had become so shriveled up by an investing "false membrane" that intestinal obstruction and death resulted. The investing membrane covered the entire small intestine and part of the large intestine. It was grayish-white, rather strong, about 1 mm. in thickness, almost cartilaginous and translucent over most of its extent. The peritoneum was replaced by this organizing exudate and connective tissue. The process of contraction had absorbed 70 to 80 per cent of the length of the small intestine; the mucous membrane had correspondingly been puckered up into transverse folds so that the lumen was practically obliterated. When the "false membrane" was divided by numerous transverse cuts, the corresponding part of the intestine could be pulled out to its original length and the infolding of mucous membrane disappeared.

The etiology was not understood. No similar condition had been seen by those who studied the case. Dr. Welch's pathologic diagnosis was "Chronic organizing peritonitis of unrecognized etiology; intestinal obstruction resulting from numerous transverse infoldings or constrictions of the intestinal wall, these being held in place by bridges of dense organizing false membrane."

The uncanny thought of a contracting investing membrane slowly shriveling up one's intestines until he must die, naturally made a vivid impression on those who saw the

* Read before the New York Surgical Society, December 13, 1922. Reprinted from *Ann. Surg.*, April, 1923.

specimen, and each one probably hoped he would never see a similar case.

My own turn for the similar case came thirteen years later.

CASE REPORT

Male, aged forty-six, No. A18153, on May 11, 1921, was transferred from the medical to the surgical division of The Roosevelt Hospital. He complained of pain and a mass in the lower part of his abdomen.

His health had been good until two years before, when he had noticed the mass, believing it due to a strain from lifting. It had been moderately painful. He had suffered from constipation and had lost 22 lbs. in weight, but he had continued his work as a doorman until two days before admission. He then apparently had an attack of definite intestinal obstruction with great pain and excessive vomiting. The attack lasted for twelve hours. The pain was cramp-like and its maximum intensity was at the location of the tumor. Following it, he had bowel movements, but was so ill as to seek relief in the hospital. Routine physical and laboratory examination revealed no abnormality excepting the mass in the lower part of the abdomen about 25 by 10 cm. in its diameters, oval, dull on percussion, slightly movable, slightly tender, its center below the umbilicus. There was a distinct depression between it and the pubes.

Catheterization of both ureters, pyelograms and cystograms, and roentgenograms of the colon revealed no abnormality.

He was serving in the British Army when the mass was first noticed, otherwise no important element was found in either his personal or family history.

Operation, May 14, 1921. Eight-inch incision through the inner portion of the lower part of right rectus. Peritoneum could not be distinguished as a definite layer. Numerous indefinite thin portions of tissue which apparently represented peritoneum and which had evidently been the seat of some form of inflammation were present. These encased a lobulated irregular mass which was about 24 cm. long and 10 cm. wide. It was a long time before its nature could be made out. In its posterior wall, there was a small calcareous nodule.

On delivering it little by little and separating the adventitious pseudoperitoneum, the retroperitoneal space was exposed. It was finally found that the tumor was composed of convoluted and adherent small intestine bound into an irregular mass by some peculiar pathological process.

The intestine which entered it from above looked fairly healthy but was moderately distended. The terminal 20 cm. of the ileum emerged from it below. It was manifest that life could not continue with the intestine thus obstructed, and hence the mass was removed after clamping and cutting the intestine above and below. The upper (afferent) intestine was adherent to the right kidney and was separated from it with considerable difficulty. Its open end was then inserted through the wall of the ascending colon near the caput coli, forming an end-to-side anastomosis, secured by two rows of stitches. The open end of the lower (efferent) intestine was inverted and secured by purse-string sutures.

FIG. 10. Tumor composed of four-fifths or more of the small intestine, shortened, convoluted and angulated by a dense, investing fibrous membrane.

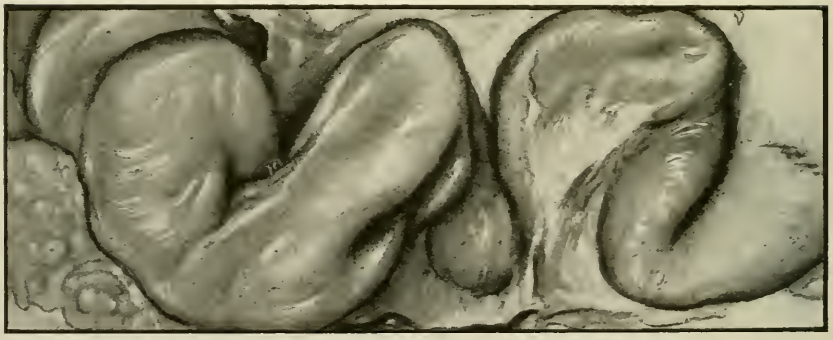

FIG. 11. A portion of the intestine pulled out so as to show the appearance of the convolutions.

The patient did well for a few days, then a leak occurred at the site of the anastomosis. Thin fluid with much digestive power leaked away and on the thirty-third day he died of inanition.

The appearance of the mass after its removal is shown in Figure 10.

Gross Pathologic Report. It was lobulated, mostly firm in its consistency, but soft in some spots. It was composed of constricted, convoluted, angulated small intestine and shriveled mesentery, all bound together by dense adhesions and bands of fibrous tissue (Fig. 11). When cuts were made into the intestine it was impossible to follow its lumen far on account of the angulations. In the mesenteric border there were some calcareous nodules.

FIG. 12.

FIG. 13.

FIGS. 12 and 13. Cross section of the intestine, showing the lumen almost occluded. Short section of intestine cut longitudinally and opened so as to show the folds of puckered mucous membrane.

When the intestine was cut across it was seen that the puckered mucous membrane nearly filled its lumen, as shown in Figure 12. The appearance of the folds of mucous membrane is shown in Figure 13. Apparently the contracting fibrous tissue outside the main intestinal wall had puckered and infolded the mucous membrane within. This appearance corresponded closely to Dr. Welch's description, but this infolded mucous membrane was not so firm nor was the investing membrane so definite as in his case. The investing membrane was irregular in its contour and could not be stripped off as a definite sheet. Nor was it possible to restore the intestine itself to its original length by making multiple incisions in this membrane, since it was too adherent to the intestinal wall to be satisfactorily separated. There was, however, a sausage-like feel to the intestine where its lumen had been filled up by the puckered mucous membrane. Those who saw the original specimen estimated that three feet or possibly a little more of the intestine had been removed. This was manifestly a very defective estimate. Unless the intestine was con-

genitally short some fifteen or more feet of its length must have been shrivelled into this contorted specimen. This corresponds to the statement of Porter and Welch that 70 to 80 per cent of the intestinal length in their specimen had been absorbed by this process of contraction.

Autopsy Report. A limited autopsy was permitted through the site of the operation incision. It was reported that the peritoneal cavity had been completely obliterated. At the site of the anastomosis between the jejunum and the ascending colon there was a small leak (5 mm. wide) with necrotic tissue about it. The length of the intestine above the anastomosis was only 16½ in. The stomach, liver, pancreas, spleen and kidneys were not removed but their size and position were apparently normal.

FIG. 14. Longitudinal section of intestine (low power) showing investing membrane and the mucous membrane raised into transverse folds. A. Investing fibrous membrane. B. Longitudinal muscular coat. C. Circular muscular coat. D. Submucous layer. E. Blood-vessels in submucosa. F. Folds of mucous membrane.

It is believed that digestive quality of the fluid in the upper part of the jejunum was an element in the breaking down of the anastomosis and in the necrosis about it.

It is surely most remarkable that this pathological process could have contracted the greater part of the small intestine into a firm mass not much larger than two good fists.

Sections were cut from the intestinal wall; the microscopic slides are depicted in Figures 14, 15, 16.

Microscopical Report. By Dr. Wm. C. White and Dr. Charles W. Lester, Roosevelt Hospital, May and June, 1921. History number A18153. Pathological number S A8924. Sections were cut through the intestine both longitudinally and transversely at (1) the portion whose lumen was practically occluded, (2) various more proximal portions whose lumen was patent but where the intestine was coiled by a veil of adhesions.

1. The section through the portion whose lumen was occluded shows all four intestinal coats. The peritoneal coat was thickened and fibrous, in some places being 1 mm. in thickness. Numerous engorged blood-vessels were present in this layer. There was no evidence of tubercle formation.

The muscular layers were separated by a thickened fibrous layer. Otherwise the appearance was essentially normal.

The mucosa and submucosa showed the most marked changes. The mucosa was apparently very redundant, and extended into the lumen in great papillae,

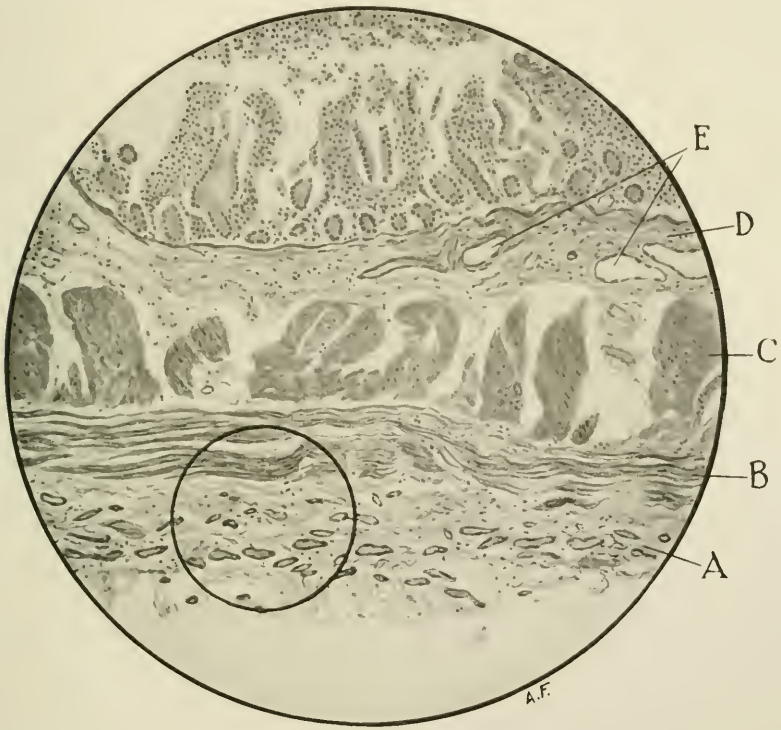

FIG. 15. Higher magnification. Portion of intestinal wall shown within small circle in Figure 16. Lettering same as in Figure 14.

like exaggerated valvulae conniventes. These were rather tortuous in their course and were so extensive as nearly to fill the lumen of the gut. The valvulae were supported by a vascular connective-tissue core derived from the submucosa. The muscle tissue did not enter into this formation at all. The epithelium and glands formed the usual villae and were normal in appearance.

2. The sections through the coiled loops of intestine with patent lumen showed a muscularis essentially the same as in the portion just described. The mucosa and the submucosa, while somewhat redundant, were not nearly so

much so as in the distal occluded portion. There were a few exaggerated valvulae conniventes, but for the most part the mucosa closely approached the normal. The peritoneal coat, however, was thicker and in addition was connected with a loose fibrous tissue which bound together the adherent coils. Sections of the investing membrane were stained by the Ziehl-Neelson-Gabbett method and searched for tubercle bacilli—none were found.

Diagnosis 1. Chronic plastic peritonitis.
2. Redundancy of intestinal mucosa.

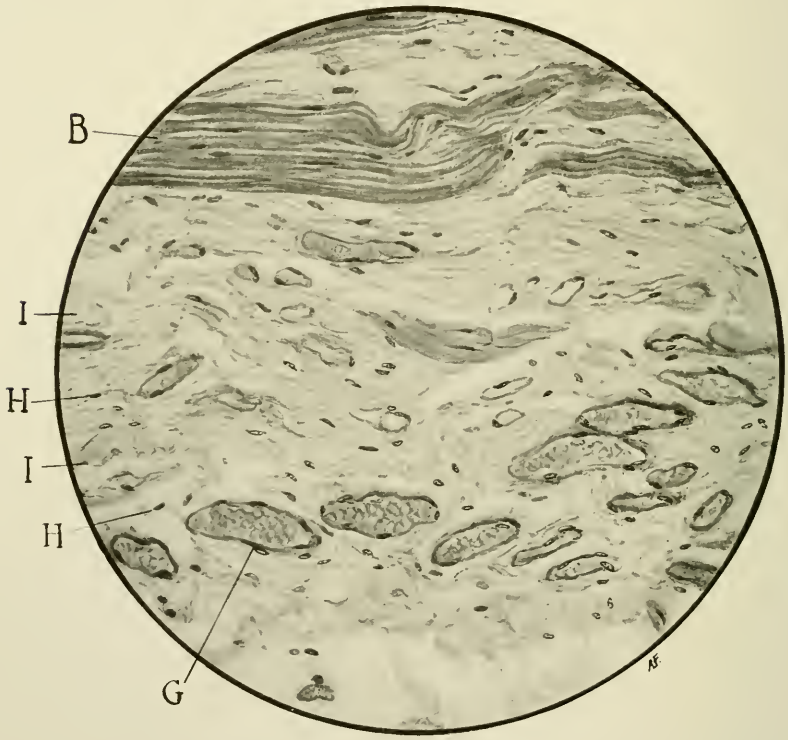

Fig. 16. High magnification of the portion of fibrous investing membrane and longitudinal muscular coat shown within the small circle in Figure 15. G. Blood-vessels in fibrous investing membrane. H. Small round cells. I. Fibrillar connective tissue.

The condition was so unusual that it seemed desirable to have the literature searched for similar cases. Dr. Charles W. Lester has spent many hours in such search, mostly under the heading of "Chronic peritonitis" and "Intestinal obstruc-

tion." The case which most resembled this was reported by J. C. Muir.[2]

Female, fifteen, who was operated upon for partial intestinal obstruction, had a mass of tangled coils of intestine resected. The peritoneal coat of the gut was thickened and inflamed with many small tubercles present; however, did not have the appearance of tuberculous peritonitis. The adherent portion was resected to within about 2 in. of the ileocecal valve, and an end-to-end anastomosis done. When the resected portion was straightened out it was estimated to be 4 ft. in length. Ten weeks later she died of inanition, and at autopsy it was found that the remaining small intestine from the pylorus to the ileocecal valve measured only 17 in. The peritoneum was thickened and showed the spots which are described as tubercles, but they did not show tuberculosis on microscopical examination.

Osler and Nicholls have given the best pathological descriptions which we have found. Osler[3] in his "Principles and Practice of Medicine," in the chapter on "Proliferative peritonitis," in which he refers to polyserositis, states that "there are instances of chronic peritonitis in which the mesentery is so shortened by this proliferative change, that the intestines form a ball not larger than a cocoanut, situated in the middle line, and after the removal of the exudation, can be felt as a solid tumor. The intestinal wall is greatly thickened and the mucous membrane of the ileum is thrown into folds like the valvulae conniventes."

Adami and Nicholls[4] writing of chronic hyperplastic peritonitis state that "the mesentery may also be shortened so that the intestines lie in a ball close to the vertebral column . . . Occasionally there is no fluid exudate and the whole abdominal cavity is obliterated by adhesions of the visceral and parietal layers of peritoneal membrane."

Nicholls[5] also in an important paper before the American Medical Association calls attention to "a peculiar form of chronic peritonitis of progressive development, several instances of which have come under my notice recently. The feature, however, that gives the affection its characteristic form is a peculiar overgrowth of fibrous tissue on the peritoneal membrane and the surfaces of the abdominal viscera, leading to induration and deformity. This fibrous tissue undergoes hyaline transformation so that plaques or continuous sheets of pearly white cartilaginous appearance are produced in various parts. The material in question has

every feature of newly formed tissue, and the disease is both chronic and progressive. Shrinkage of the fibrous tissue takes place, hence one might correctly speak of the disease as chronic indurative peritonitis." The process is usually most marked about upper part of peritoneal cavity, liver, spleen, omentum, mesentery and may even extend to the pleural and pericardial cavities. "Although not new, the subject is one that has attracted but little attention in proportion to its importance. Ascites usually calls clinical attention to it, and somewhat resembles cirrhosis of the liver."

The quotations from Osler, Adami and Nicholls are under the headings of some form of chronic peritonitis, but these authors in the same connection refer to a particular form of chronic peritonitis which is combined with inflammation of other serous membranes—especially the pleura and pericardium.

This form of inflammation has been distinctive enough to receive an especial name, in fact several names have been given to it. Nicholls[6] calls it multiple progressive hyaloserositis and definitely refers to it in the above quotation. The subject is so intimately associated with our localized intestinal peritonitis that is should be described before proceeding further.

Chronic Multiple Serositis. For at least three-quarters of a century surgical and medical literature has contained occasional references to this peculiar inflammation of the serous membranes, slow in its progress and leading to the formation of firm layers of fibrous tissue where the serous membranes had previously been and in certain localities to the adhesion of opposing serous surfaces.

The most common sites of this inflammation have been in the abdomen, especially in its upper part, in the pleural cavities and in the pericardium. The inflammation in the upper part of the abdomen has led to the adhesion of the upper surface of the liver to the diaphragm and to the encasement of the liver and sometimes of the spleen in a "firm membrane which is composed of dense layers of connective tissue of a peculiar cartilaginous appearance." This fibrous encasement has been very firm. The inflammation in the pleura has led to the obliteration of part or all of one or both

pleural cavities. The inflammation in the pericardium has caused the obliteration of the pericardial sac and in at least one instance (Kelly[7]) this process has gone to the stage of calcification so that a large section of the heart has been encased in a calcareous sheath.

Various names have been applied to this condition: Multiple progressive hyaloserositis (Nicholls); Chronic deforming perihepatitis; Zuckergussleber (icing liver) (Curschmann); Pericarditic pseudocirrhosis of the liver (Pick); Multiple serositis (Kelly); Chronic multiple serositis (Mayo).

It is noted that the liver is referred to in many of these descriptive titles. The encasement of this organ in a dense layer of fibrous tissue is a prominent part of this remarkable pathological process. Pick's name is often used in describing the disease, although most observers ascribe less importance to the pericardial inflammation than he does. Curschmann's name is also frequently used in connection with the term "zuckergussleber."

Ascites has been the most prominent symptom. Many of the patients have had the ascitic fluid withdrawn time after time, 301 times in one instance. It is believed that many patients with supposed cirrhosis of the liver have really had this form of serositis. Symptoms referable to the heart and to the pleura have been next most common. The disease has been chronic and patients have gradually lost strength, the character of the symptoms depending on the site of the maximum inflammation.

The disease is a rare one, although Nicholls believes it not quite so rare as is generally supposed. Since ascites is the only symptom which has ordinarily led to a diagnosis, it is manifest that in the absence of ascites a considerable degree of inflammation could exist without the making of a diagnosis.

The resemblance between this condition and tuberculous peritonitis has caused considerable confusion. Picchini,[10] in considering 110 cases under the term "Polionomenite," really refers to tuberculous peritonitis in most instances, and Concato[11] has reported on "Polionomenite scofulosa." In 1903 Kelly,[7] in a masterly résumé of the subject, using the title "Multiple serositis," tabulated 39 cases, at least 8 of which were tuberculous. Nicholls states that "it is quite possible for

the tubercle bacillus to produce a hyaline and productive fibrosis of the peritoneal membrane quite comparable to the simple form previously described" and quotes cases of Strajesko and Herrick for examples.

It is noteworthy that a disease which is characterized by the formation of extensive firm layers of fibrous tissue within the abdomen should interfere so little with the intestinal function, or at least that there should be so few reports of such interference. These fibrous layers are located mostly in the upper part of the abdomen, but there seems to be no natural line of demarcation between that and the lower part of the abdomen. Where there is so much of this fibrous tissue above we would naturally expect some below. As a matter of fact, we do find continual reference to such deposits. Kelly states of his case, "The coils of intestine are united to one another and to the other intraabdominal organs by moderately firm though friable fibrinous adhesions. In some places an exudate may be stripped off in thin layers." In his tabulation of 39 cases, there are many references to adhesions in various parts of the abdominal cavity. This year Mayo[12] called attention especially to the abdominal manifestation of "Chronic multiple serositis," in a paper read before the American Surgical Association. He referred to a patient who, in addition to the glistening white membrane in the upper part of the abdomen, also had the area of the small intestine "surrounded by a sheath of thickened peritoneum which bound the intestine down to the spine and resembled the flattened crown of a derby hat."

Nicholls describes a case in which, in addition to the dense deposits in the pleura, pericardium and upper part of the abdomen, the parietal peritoneum was thickened, the mesentery was shortened and thickened, and "the intestines lay bunched along the vertebral column." The small intestines were short and the rugae pronounced.

Jabez Jackson,[13] in his article on "Membranous pericolitis" and allied conditions of the ileocecal region, refers to a case which has bearing on the subject. "In one instance at least the membrane was a solid sheet of fibrous tissue, perfectly opaque and entirely obscuring the entire ascending colon and hepatic flexure, which could not be recognized at

all until the membrane was divided and stripped away. Then we discovered a small, contracted, atrophied colon which we believed incapable of restored function. In this case we excised the entire ascending colon, including the hepatic flexure, and made an anastomosis between the ileum and transverse colon, thus entirely curing our patient."

Thus, in studying the reported cases we find that there is no lack of fibrous deposit about the intestines, but rather that the intestine shows a remarkable power of adjustment in continuing to function so long in spite of these constrictions. This is in marked contrast to the occasional result of local adhesions, for we all have seen angulation and complete obstruction caused by strands of fibrous tissue hardly thicker than knitting needles.

Etiology. It is generally believed that the production of this fibrous membrane is due to the action of microörganisms of low virulence. Pneumococcus, B. coli, B. typhi, B. tuberculosis, are the most likely offenders.

Without doubt many of the reported cases have been due to tuberculosis. But there is marked difference between this dense whitish cartilage-like membrane and the ordinary product of tuberculosis. Nicholls has described a case in which he believes the inflammation came from the gall-bladder and believes that this is not an uncommon source of the infection. He believes that the lymph spaces are followed in the syndrome which comprises upper abdomen, pleurae and pericardium.

It is also suggested that the formation of this membrane is due to toxins which are developed within the liver or within other abdominal organs. With our present knowledge it is manifestly impossible to prove such an hypothesis. We may well agree with the statement that Dr. Welch made in a discussion of Dr. Nicholls' paper to the effect that the "etiology is very obscure."

SUMMARY

1. There are a few recorded cases of chronic peritonitis which has agglutinated the small intestines into relatively small globular masses.

2. The intestinal mucous membrane becomes puckered into folds and eventually occludes the intestinal lumen.

3. The outside appearance of this mass gives little indication of the real length of intestine which it contains. Four-fifths of the small intestine may be contracted into a mass which apparently contains about one-fifth.

4. The cause of this peritonitis is not definitely known, but it is believed to be due to a low grade of infection or to the toxins of such infection. In certain instances the inflammation may have been tuberculous.

5. There are many points of resemblance between this process and inflammation known as chronic multiple serositis. Indeed, similar intestinal peritonitis has in certain instances formed a part of chronic multiple serositis.

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THE SURGICAL TREATMENT OF MEGACOLON*

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IT is nearly a century since Parry described a case of megacolon observed at autopsy, in an adult who had suffered from digestive disturbance for years. This colon was enormously distended, and contained an immense quantity of feces. We do not know what observations had preceded his, but between 1825, the date of his publication, and 1886, the date of Hirschsprung's first article, there were at least twenty-six publications about these tremendously enlarged colons. Hirschsprung's articles stimulated attention to the subject and they came at a time when abdominal surgery and abdominal pathology were receiving increased attention; hence when Finney wrote his classical article in 1908 he found a bibliography of 206 articles. Since that time the literature has increased even more rapidly, and is now so large that it is hardly possible to grasp it in full detail.

Method of Occurrence. Congenital idiopathic dilatation of the colon (Hirschsprung's disease) has generally been considered, in large degree, a disease of childhood. There are a great many descriptions of the disease occurring in children. They surely make the most vivid pictures. Hirschsprung advocated the name of "true" megacolon for them and the name of "pseudo" megacolon for those cases occurring in adults. With the later development of the subject this distinction has not always held. Many observers believe that if some patients with this disease can worry along to adolescence, others can reach adult life and that there is no proper age limit. The subject has been complicated by the including of reports of localized megacolon. Even in the undoubted congenital cases the sigmoid is more apt to show dilatation than the rest of the colon: the intestine angulates at the fixed points and distends elsewhere, although after its removal it

* Read before the American Surgical Association, June 14, 1921. Reprinted from *Ann. Surg.*, Oct., 1921.

may be as large at a point of former angulation as at a point of former dilatation: hence it is not strange that there should be many reports of localized megacolon. However, the custom of reporting such cases has led to the description of an increased number of adult cases, and an increased proportion of cases in whom the mechanical factor of obstruction predominates. Hence considerable confusion has resulted, and it is now impossible to differentiate in the literature those patients in whom the enlargement of the colon is due to a congenital defect from those in whom it comes from mechanical or spasmodic obstruction. We know, however, that enormously dilated and hypertrophied colons are observed in children, and that similar conditions are sometimes seen in adults; also that the adult cases in the main show greater evidence of mechanical or nervous obstruction as causative factors.

Pathology. The degree of dilatation which these colons reach is almost beyond belief. Finney states that the circumference of the abdomen may be greater than the height of the patient and quotes Peacock as describing a colon which contained sixteen liters. Graves describes a colon 110 cm. long and 31 cm. in circumference in its descending portion. Bensandi and Sorrel describe one 26 cm. in circumference. Johnson describes a colon which contained three or four quarts of feces. From the second case recorded in this paper at least one gallon of semifluid feces was withdrawn on the operating table, and about another gallon drained away in the next two days. The removed portion of the colon in Case 1 easily held four liters of fluid after its removal. The walls of the colon are usually hypertrophied as well as dilated, especially in their circular muscular coats. The mesocolon may be lengthened and hypertrophied in all its elements. Obstructive valves have been described. Volvuli have been found. A few anal fissures have been described giving suggestion of spasmodic obstruction above.

Etiology. There are three main theories for the etiology:

1. That it is due to congenital defect in the development of the colon.

2. That it is due to some form of mechanical obstruction, and that the colon hypertrophies and dilates in its efforts

to overcome this obstruction, just as the heart hypertrophies and dilates when increased demand is made upon it.

3. That it is due to spasm of the circular fibers in the lower part of the intestine, and that dilatation of the colon follows this spasm just as dilatation of the esophagus follows cardiospasm, or dilatation of the stomach follows pylorospasm.

It is altogether probable that two or more of these elements are active in many of the cases.

Symptoms. The main symptoms are abdominal distention, constipation lasting sometimes for very long periods, intermittent diarrhea, loss of appetite, emaciation, apathy.

The study of the treatment of the disease is the main purpose of this paper. Very careful consideration of its occurrence, pathology, etiology and symptoms is given in other papers, particularly that of Finney, to which readers are referred for such information.

RECORD OF CASES

Case 1. Female, aged ten and a half. Roosevelt Hospital, No. A16873. First seen by writer March 31, 1920. She had reasonably good health during the first seven years of her life, then loss of strength and listlessness. At eight and a half years irregular attacks of abdominal pain began, in epigastrium and on both sides. They were accompanied by constipation. Her disability progressed; by December, 1919, she had become a real invalid, taken about from one doctor to another in search of relief from her distress, weakness, pain, alternating constipation and diarrhea and frequent micturition.

When admitted to the hospital she was found to be a thin, emaciated child of 61 lbs., having a very large abdomen. The left half of the abdomen contained a large, rather soft, slightly movable mass. Enemas brought away an enormous quantity of feces and the mass disappeared. No obstruction could be found in the rectum. *X*-ray examination after a barium enema showed a dilated sigmoid (Fig. 18). It was not found practicable to give enough barium mixture, either by mouth or rectum, to secure a picture of the entire colon in a dilated condition.

Operation. After ten days of further treatment by medicine, diet and enemas an operation was done. A 7-in. incision was made through the inner part of the left rectus muscle; a greatly distended transverse and descending colon were immediately encountered. They seemed to fill the greater part of the abdomen and to push the rest of the intestines backward and to the right. The splenic flexure was held in position by its peritoneal attachment, the costo-colic ligament, and formed an acute angulation. The distention seemed largely due to gas.

The descending colon and the splenic flexure were mobilized by dividing their outer leaf of investing peritoneum. The mesocolon was then divided in

sections from the lower sigmoid to the hepatic flexure. The liberated loop of intestine, somewhat over 40 in. in length and 4 in. or more in diameter, was then drawn outside of the abdomen through an intramuscular incision which had been made for that purpose above the left anterior superior iliac spine.

FIG. 17. Diagrammatic drawing showing condition of megacolon in Case 1. Colon angulated at splenic flexure. Transverse colon and descending colon and sigmoid flexure greatly distended.

This brought the hepatic flexure into contact with the lower sigmoid without undue tension. The afferent and efferent intestinal walls were stitched together within the abdomen to aid in proper "spur" formation. The median wound was

FIG. 18. Roentgenogram after enema of barium mixture showing shadow of the descending colon and sigmoid flexure.

FIG. 19. Roentgenogram taken twenty-four hours after meal of barium mixture showing condition of colon three months after operation.

then closed and sealed. The intestine at the place of exit was secured to the abdominal wall. Temporary circular ligatures were applied to it outside of this exit and the loop of colon beyond the ligatures was ablated. The ablated portion was 95 cm. long and held 4 liters of fluid when injected.

Patient showed considerable shock and reaction after her operation, but finally rallied satisfactorily. The temporary circular ligatures were removed from the protruding stumps of intestine after forty-eight hours and a "double-barrelled" intestinal stoma was thus established.

The median incision healed by primary union. The clamping of the spur was begun after twenty-five days, and twenty-three days later the intestinal ends were stitched together at the site of the stoma.

She left the hospital seventy-eight days after the operation. At that time the stoma was firmly closed. She was having normal bowel movements; she had been walking and playing about the ward and the porch for two or three weeks; she ate well, had gained much strength, and $5\frac{3}{4}$ lbs. in weight. The roentgenogram shown in Figure 19 indicates the condition of the remaining colon at that time.

She has been carefully followed during the intervening months. Her digestion has remained normal, and she has normal daily stools. She has gained 12 lbs. in weight since she left the hospital, and is now a normal, active, happy, good-natured youngster.

A roentgenogram taken March 7, 1921 shows that the colon has about the same outline as when she left the hospital.

Pathological Report

Macroscopic (Dr. W. C. White). Specimen consists of a piece of large intestine 95 cm. long, in transverse diameter varying from 5 to 7 cm. The wall is thin, markedly dilated, pale and of atonic appearance. The mucosa appears normal and the specimen otherwise is unremarkable.

Microscopic. The entire wall is very much thinned out. The mucosa is intact and shows no inflammatory reaction. The muscularis mucosae is very thin. The submucosa consists of relatively loose tissue. The circular and longitudinal muscles are thinned out. The serosa is loose and shows no connective-tissue increase.

Case II. Female, aged seventeen. Roosevelt Hospital, No. A1733. Admitted November 6, 1920. She had always been very constipated, has had three or four attacks of great abdominal distention and vomiting during her life. The last previous attack came six months ago; the distention then was almost as great as at the present time. She then had repeated vomiting and severe abdominal "cramps."

The present attack began three weeks ago with abdominal distention, nausea and vomiting. The distention increased and was accompanied by very severe abdominal pains. Repeated enemas had been given, but some of them at least did not return. The bowels, however, had moved two or three times a day much of the time. During the past three days she had many times vomited green offensive material. Had been in bed the entire three weeks and had become very weak.

On admission to the hospital she was emaciated, very feeble, pulse 140, abdomen enormously distended. The outlines of the intestine were visible through the thin abdominal wall, and slowly moving peristaltic waves could be seen. Enemata and rectal tubes were used in an effort to empty the bowel, but they were not successful. Operation was therefore done.

Through an incision in the lower part of the left rectus muscle an enormously distended sigmoid flexure was found. It was about as tense and thick-walled as an ordinary large ovarian cyst. It could be traced from the pelvis to the upper left angle of the abdomen, but satisfactory examination of the colon beyond that point was not practicable. A suction trocar withdrew semi-solid feces. A purse-string suture was placed about the trocar wound. The abdominal incision was closed except an opening of $1\frac{1}{4}$ in.; the intestine outside the purse-string was stitched to the edges of this opening, a flanged glass tube was introduced within the purse-string and secured in its position. About one gallon of fecal material was then drawn through the tube by a suction apparatus. During the following forty-eight hours about another gallon of fecal material drained away. The abdomen became flat, its circumference was reduced from 34 to $26\frac{1}{2}$ in.

For a few days she showed some recuperative power, but died on the sixth day after her operation, apparently with a low grade of pneumonia. She showed no signs of peritonitis. Autopsy was not allowed.

Case III. Male, aged forty-two. Admitted to the First Surgical Division of the Roosevelt Hospital, April 21, 1921. He had suffered from various forms of digestive disturbance during much of his life. Appendectomy was done in 1909. Gastroenterostomy was done in 1912. He had then enjoyed reasonably good health until two weeks before admission to the hospital when he had an attack of bronchitis or bronchopneumonia. Sixty hours before admission he was seized with very severe general abdominal pain—"doubled up with the cramps." Vomited repeatedly—attacks of vomiting and pain have both continued until the present time. Constipation "very bad" for the past two weeks. Bowels did not move without catharsis, and then only in small quantities. Much worse since pain started. No gas per rectum. When admitted to the hospital he seemed weak, thin, very ill, and in much pain. His abdomen was distended, there was much muscle spasm, and dullness at its lower part. Peristaltic waves were visible.

Operation. Four-inch incision in right rectus, enlarged to 6 or 7 in. Abdominal contents under much tension. Small intestine collapsed and apparently empty throughout its entire extent. In the left side of the abdomen, extending from the diaphragm into the pelvis, there was an enormously dilated portion of the large intestine. In order to deliver this it was necessary to remove the small intestine from the abdomen. They were temporarily confined in warm moist towels; the distended colon was then found to extend from the ileocecal valve to the beginning of the transverse colon; it was delivered with considerable difficulty. The large intestine below the middle of the transverse colon was not dilated. The constriction seemed to have been caused by hinging of gut at the middle of the transverse colon. The entire ascending colon had been transferred to the left side and had become enormously dilated in that position. An effort was made to push the gas downward from the dilated

intestine. This was only partially successful although no definite band of constriction could be found. A rectal tube was inserted through the anus to aid this procedure. The outer layers of the dilated intestine were dark in color and the wall had broken down in several places. It was therefore deemed wiser to leave it outside the abdomen than to make further efforts to return it. The wound was therefore closed in layers to the emergence of the intestine. The distended intestine was then punctured with an aspirating trocar and a large amount of gas withdrawn, also some very foul-smelling fecal material. The afferent and efferent legs of the intestine were sewed together. The intestinal wall was stitched to the skin. Wound was smeared with sterile vaseline. The ascending colon, which was still somewhat dilated, was left in the dressing and the patient returned to bed in this condition. After two days a part of the protruding intestine was excised and sent to the pathological laboratories.

Pathological Report

Macroscopic. Specimen consists of an opened and somewhat dilated cecum preserved in formalin. It is more or less cylindrical in shape and measures 13 cm. in the longitudinal axis and varies from 2.5 to 6.5 cm. in transverse diameter across the opened surface. The serosa is rough and has some adhesions. The wall everywhere is thickened, measuring in many places 1.4 cm. It is firm and fibrous. The mucosa is smooth and thrown into folds. There are no areas of ulceration, necrosis or hemorrhage. The lumen is patent and varies from 2 to 5.5 cm. in transverse diameter.

Microscopic. The mucosa is about the normal in thickness, but the submucosa is greatly increased with newly formed connective tissue. The submucosa is vascular and has a round-cell infiltration throughout. The circular muscle is about three times as thick as that shown in Case 1, but the longitudinal is about the same in thickness. The serosa is greatly thickened and shows a chronic inflammatory reaction.

He did well. The wound healed firmly to the emergence of the intestine. Clamps were applied to the spur on May 25th. On May 31st the ends of the intestine were sewed together. At the present time he is still under treatment in the hospital.* He is doing well and is gaining steadily in strength. The stoma is not yet entirely closed.

These 3 cases illustrate various phases of the problem. Case 1 shows the good result which may come from the removal of a sufficient portion of the enlarged colon. Case II shows that a patient with this disease may drift along beyond the possibility of relief, either medical or surgical, and that this drifting may occur while she is trying to attend to the ordi-

*Later note. He left the hospital in good condition with stoma entirely healed on July 20, 1921.

nary duties of life. Cases I and III both illustrate the comparative safety of the extraperitoneal two-stage method of resection (Mikulicz). The cases, however, are too few for general deductions. They are only to be considered in conjunction with the extensive literature which now exists.

Consideration of Literature. As a starting point it should be stated that this literature gives abundant proof that surgical treatment is more successful than medical treatment. For instance, Duval gives 74 per cent mortality from medical treatment, 34 from surgical treatment; Lowenstein, 66 from medical, 48 from surgical. Ladd has given the following tabulation of 118 cases:

	Total	Cured, per cent	Improved, per cent	Unimproved, per cent	Died, per cent
Treated medically.....	60	12	13	6	67
Treated surgically.....	58	41	8	3	41

Terry found a mortality of only 27 per cent in 95 cases treated by surgery. Neugebauer, quoted by Hubbard, referred to 123 cases treated medically with only 1½ per cent of cure.

Surgical Treatment. The term surgical treatment is a very elastic one and includes many forms of procedure. It is interesting to know how different surgeons have met the problems of this disease; it is also important to know the results of the different forms of treatment which they have used.

A number of tabulations have been made but we know of none which give the statistics of a large number of cases treated by modern surgery. Hence, with the aid of Dr. Charles W. Lester, the literature has been searched for records of operations since 1908, the time of the publication of Finney's article. The search has been carefully made, and without doubt most of the published reports have been found. Some have probably escaped notice, but no report which has been found has been omitted. One hundred and forty-three cases have been tabulated. This includes 136 cases found in the literature, 4 learned of by personal report, and the 3 recorded in this paper.

TABLE 1

RESULTS OBTAINED IN 143 CASES OF MEGACOLON TREATED SURGICALLY BETWEEN 1908 AND THE PRESENT TIME

	Total	Cured	Improved	Unimproved	Died.	Mortality Rate per cent
One-stage resection	42	28	3	..	11	26
Two-stage resection intra-abdominal method	31	23	2	1	5	16
Two-stage resection extra-abdominal method (Mikulicz)	13	11	1	..	1	8
Colostomy, cecostomy, appendocostomy	20	3	4	..	13	59
Short-circuiting	22	13	..	2	7	32
Colon plication	2*	2				
Colopexy	3*	2	1			
Colon plication and colopexy	1*	..	1			
"Laparotomy"	1	..	..	..	1	
Laparotomy with massage of colon	2	..	..	..	2	
Incision of stricture	1	..	..	1		
Release of volvulus	4*	3	..	..	1	
Colotomy	1	..	1			
Total	143	85	13	4	41	28.7

* Other patients who had secon lary operations when these procedures had failed to cure are grouped under "two-stage" resections; hence this tabulation does not show the failures of these semipalliative operations.

This table shows an improvement in the general mortality rate. So far as I know 28.7 per cent is a lower mortality rate than has previously been reported for a large collection of cases, excepting Terry's report of 27 per cent. The mortality rates shown in some previous tabulations are here given:

	Date	Number of cases	Mortality rate
Lowenstein	1907	44	48
Schmidt	1908	71	48
Duval	1910	..	34
Schneiderholm	1915	143	36
Ladd	1921	58	41

The improvement seems to be due to the more general use of rational radical surgical procedures. The increase of

such surgical procedure is strikingly shown in comparing the table given above with that prepared by Schmidt in 1908 (see addenda). It is noteworthy that although Schmidt's tabulation contained only five two-stage resections intraabdominal and extraabdominal they were all followed by recovery.

From a surgical standpoint the cases may be divided into three groups:

1. Those for whom only colostomy or appendicostomy was done.

2. Those for whom there was only some semipalliative procedure such as short-circuiting, colopexy, relief of volvulus, colon plication, etc.

3. Those for whom more or less of the colon was resected.

Group 1. The first group should hardly be considered surgical. If patients drift along into semimoribund condition, and then apply to a surgeon for relief of obstruction, they show the ill effects of whatever treatment they have previously had. If the surgeon is magnanimous enough to try to relieve their condition by colostomy he makes a praiseworthy effort to save life, but he has not had a reasonable opportunity of curing megacolon by surgery. It is not strange that there was a 59 per cent mortality among the 20 patients in this group. That mortality, however, cannot fairly be considered surgical. Of course this group does not include those cases in which the colostomy was the first step in a two-stage operation.

Group 2. Semipalliative operations of the type here mentioned were common in the earlier reports. In this tabulation they represented less than 26 per cent of the total. Surgeons now prefer procedures which give more prospect of permanent cure. The mortalilty rate of this group is ⁻ per cent higher than for the combined three groups of resections, and the records of "cures" are 18 per cent less. Secondary operations were frequently done on patients who had previously had one of these semipalliative procedures, but such cases are recorded under two-stage operations.

Group 3. *Partial Colectomies.* At the present time the main surgical interest centers in the problem of removing as much of the enlarged colon as is practicable, and this is

the obvious procedure. There are three main methods of doing this:

(*a*) In one stage, removing a portion of the colon and uniting the divided ends within the abdomen either by end-to-end, end-to-side, or lateral anastomosis.

(*b*) Using two stages for intraabdominal resection. There are many variations of the intraabdominal two-stage method —a preliminary colostomy may provide for washing out the colon before the resection, and may provide a vent afterwards. The cecostomy or appendicostomy may be done for a vent at the time of the resection. A short-circuiting may be done first and a removal of the excluded intestine later. A release of a volvulus or colopexy or colon plication may be done first and a resection later.

(*c*) An extraabdominal resection may be done in two or more stages. The portion of colon which is to be removed may be mobilized and delivered outside the abdominal wall before it is opened, preferably through a separate incision; after stitching the intestine to the abdominal wall and closing the primary incision completely and the secondary incision to the point of emergence of intestine, the lumens of the gut are temporarily closed and the desired portion of colon ablated. The continuity of the intestine is later established by removing the spur and sewing the ends of the intestine together.

The dangers of these procedures diminish in the order given. The table gives the mortality rates as 26 per cent for one-stage resection, 16 per cent for intraabdominal resection in two stages and 8 per cent for extraabdominal resection in two or more stages (Mikulicz). These rates may vary with the next table made, but they correspond in fair measure with other statistics.

Each surgeon will endeavor to fit the procedure to the individual case. The proportion of cases of real megacolon which are suitable for a one-stage resection must be small. The main dangers come from sepsis and shock. These colons are particularly foul. No doubt some of them can be so cleansed as to make one-stage resection justifiable, but most of them will need some provision for possible infection or leakage at the site of union and possibly a vent for escape of

gas from another part of the intestine. The manipulation incident to a one-stage resection is often more than these patients can endure. A simple time-saving procedure is very desirable.

If operation in two stages is decided upon, each surgeon will again endeavor to fit the procedure to the individual case. Extraperitoneal resection (Mikulicz) is often more tedious and trying to patient, nurse and surgeon than other forms of two-stage operations. It has never been generally popular, as is shown by the limited number of reported cases. It is, however, becoming more popular and is a very valuable resource; it is doubtful, for instance, if Case 1 would have survived and obtained so good a result under any other form of operation. It has the great advantages of rapidity, diminished manipulation of the intestine and diminished shock to the patient. It gives less likelihood of troublesome adhesions. The danger of infection is very greatly diminished since the portion of intestine which is to be ablated is delivered outside the abdomen before it is opened.

It is quite possible that further development of the two-stage intraabdominal method may meet these advantages; that the colon may be adequately cleansed; that suitable provision for possible leakage at the suture line may be made and that an intestinal vent may be provided which will prevent the accumulation of gas. Also that the patient's strength may be so conserved as to provide a reasonably safe margin for extensive operation.

It is, however, to be remembered that most of these operations are done under adverse conditions. The patients are weak and debilitated, the procedure is an extensive one, the resources of surgery are put to a maximum test and the procedure which gives the least danger must often be selected, even if it implies a more disagreeable convalescence than one would wish. Hence the two-stage extraabdominal method (Mikulicz) is our safest resource for a larger proportion of these patients.

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This consists of those cases of megacolon from which Table 1 was prepared. They were treated by operation between 1908 and the present time. The bibliography and the tables in the addenda were prepared by Dr. Charles W. Lester.

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Addenda

SCHMIDT'S TABULATION OF CASES OF HIRSCHSPRUNG'S DISEASE TREATED BY SURGERY*

		Cured	Improved	Not improved	Died
Expl. lap.	11	3	2	1	5
Puncture	4	..	..	..	4
Artificial anus	10	1	..	1	8
Colotomy	5	..	..	..	5
Plication	2	1	..	1	
Colopexy	6	4	1	1	
Anastomosis (short circuit)	16	6	3	..	7
1 Stage resection	12	6	..	1	5
2 Stage resection	4	4			
Extraabdominal resection	1	1			
Total	71	26	6	5	34 = 48%

AGE OF PATIENTS RECORDED IN TABLE I

Age	Total	Cured	Per cent	Improved	Per cent	Not improved	Per cent	Died	Per cent
Under 6	27	10	40	3	12	..	..	12	48
6–10	17	10	59	..	..	2	12	5	29
11–20	21	16	76	..	..	1	5	4	19
21–40	37	27	73	3	8	1	3	5	14
41–60	22	15	68	..	..	..	..	7	32
Over 60	11	4	36	1	9	..	..	6	55
Not stated	8	7	87	..	..	..	..	1	13

PATIENTS RECORDED IN TABLE I

Cause of death	Number
Peritonitis	16
Shock and collapse	13
Embolus	4
Pneumonia	2
Hemorrhage	1
Other causes	5

* Prepared 1908. *Beitr. z. Klin. Chir.*, LXI, p. 682.

REPORT OF THE RESULTS OF OPERATION ON A GROUP OF 150 CASES OF GOITER*

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THE effort of the Executive Committee of the American Surgical Association to promote late reports on the results of treatment for goiter is surely a commendable one. There is hardly a subject which is more discussed in surgical literature than goiter; and the effort to solve the goiter problem is attracting the energies of a very large number of competent men; but in proportion to this great activity, there has been too little attention to the late results of the different forms of treatment.

Wishing to add a little to the subject, I have endeavored to study the later condition of 150 patients on whom I personally operated for goiter between 1899 and 1924. The report is confined to personal cases, because they give better opportunities for study than we are able to obtain from groups which represent the work of several surgeons on a hospital division. These represent all the patients on whom the writer has operated for goiter during this period.

In addition to these cases many others have been treated by medication, rest, hygienic regime, or *x*-ray. Most of them have passed out of observation but have shown certain peculiarities which are referred to in the text.

The types of goiter have varied from acute hyperplastic goiters of overwhelming toxicity to encapsulated cysts with little or no toxicity. Toxic adenomata, however, were more common than any other type.

There were also 2 cases of cancer which are not included in the list, because only diagnostic incisions were made.

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All but 5 of the patients have been traced since leaving the hospital. The periods of observation are indicated in the following table:

Followed into 21st yr	1 patient	Into 9th yr	9 patients
Followed into 20th yr	1 patient	Into 8th yr	13 patients
Followed into 17th yr	1 patient	Into 7th yr	8 patients
Followed into 16th yr	2 patients	Into 6th yr	13 patients
Followed into 15th yr	4 patients	Into 5th yr	17 patients
Followed into 13th yr	2 patients	Into 4th yr	14 patients
Followed into 12th yr	4 patients	Into 3rd yr	17 patients
Followed into 11th yr	3 patients	Into 2nd yr	16 patients
Followed into 10th yr	7 patients	Into 1st yr	8 patients

The reports have been made by the writer from personal observation in 83 instances; by another physician 11 times; by the patient either by letter or telephone conversation with the writer 26 times; by a nurse 6 times; by the patient's relative or friend 14 times.

Kinds of Operations. The operations have been done primarily with the view to adjusting the operative procedure to the patient's strength, but with the ultimate purpose of removing as much of the thyroid gland as the patient could spare without endangering the normal thyroid function. In most instances, four-fifths of one lobe and from one-third to three-fourths of the other lobe have been removed. A primary ligation of one or both superior thyroid arteries has been done in 12 instances. Usually this has been followed by the removal of a large portion of the enlarged gland. Occasionally no further operation than the ligation has been practicable or even desirable. As the work has progressed, it has been possible to gauge the patient's strength in such a way as to keep within fairly safe limits in the selection of operative procedure.

"*Standards for Estimating Results.*" In estimating the results of these operations, we have based the reports on the ability of the patient to perform the ordinary duties of life. We believe that this is the most important standard. The patients who come to us with goiter wish to be cured of their disabilities, so as to have at least the ordinary capacity for work and enjoyment. A result short of this is not satisfactory,

no matter what the pulse-rate, basal metabolism, or bodily weight. If, however, these patients are able to carry on the ordinary duties and pleasures of life in comfort and health, the results may be considered satisfactory.

It is important to have a mental picture of the entire group of patients; thus endeavoring to show what may be expected of such people after their operations.

We have, therefore, classified them into five divisions:

1. Operative fatalities.

2. Patients who have died either of intercurrent disease or from results of goiter since leaving the hospital.

3. Patients who are definite invalids.

4. Patients who are able to do a moderate amount of work and to enjoy life, but habitually have to guard against overexertion.

5. Patients who really enjoy life and have at least the average capacity for work or other activities.

Fortunately, the latter group preponderates in a large majority. If we consider those patients who have been observed since leaving the hospital, 73.6 per cent belong to this group. An additional 22.8 per cent are grouped with those who can enjoy and do a moderate amount of work but have to guard against overexertion.

In order to explain these divisions, we may refer to some of the patients in detail.

Division 1. *Operative fatalities*—5 patients. The first 3 had advanced Graves' disease in its extreme form. Their ages were, respectively, twenty-three, twenty-six, and sixteen years. They had exophthalmus, palpitation, sweating, extreme nervousness and very rapid hearts. One of them died on the table before even a ligation could be completed. Another died three days after operation with edema of the lungs, and the other on the third day after operation, having "rusty" sputum and signs of pneumonia.

In view of subsequent experience, operation would not have been attempted on these patients in the conditions which they then showed. These 3 fatalities occurred among the first 33 cases. It is possible that a preliminary ligation of a single superior thyroid artery at a properly selected time without even removing the patient from bed, might have

been successfully done for one or all of them and that further procedure could have been accomplished later.

It is to be noted that in the next 117 cases there were only 2 deaths. One of them, a girl of twenty-three, who had suffered from hyperplastic goiter for several years and had undergone several operations, died after an effort to remove a part of the remaining left lobe of the gland. The other was a patient who, beside her goiter, had mitral regurgitation and a dilated heart. She was kept in the hospital for twenty days before operation, and although her heart lesion was well understood, the operation seemed advisable. She went through the operative procedure without incident. Her pulse was about 90 throughout the operation and she seemed to do well until the evening of that day, when she suddenly died. The physician who observed her at that time thought that her death was due to a coronary embolus. Every surgeon who is not excessively timid has to take an occasional risk of this sort. When, however, we consider that there were 117 consecutive cases with only these 2 deaths, we may appreciate that we are dealing with a very low operative mortality.

In considering this group of fatalities, we are impressed with the deadly character of the disease in the first 4 of these patients, and our great regret is that their thyroids could not have been attacked before their hyperplasia had led to such serious symptoms.

Division 2. *Patients who have died since leaving the hospital,* either from progress of the *goiter* or from *intercurrent disease.* Four patients: One thirty-three years of age, who had suffered from goiter for seven years, and who had reached the stage of degeneration of her internal organs. She was kept in the hospital for twenty-nine days, resting in bed and having symptomatic medical treatment. Her basal metabolism varied between 64 and 39. The superior thyroids were then ligated without incident; one at a time, under local anesthesia, in her bed. She improved considerably, but insisted on going home. She died a month later in another hospital from so-called "heart disease."

The second case was a girl of nineteen years, with a moderate-sized goiter, exophthalmus, basal metabolism plus 37

and hereditary syphilis. Her two superior thyroids were ligated and she improved so satisfactorily that at one time I was willing to undertake subtotal thyroidectomy. Her guardians, however, refused this and she went from the hospital. She was under *x*-ray treatment for more than a year. She finally died with apparent degeneration of her internal organs.

The third case died about a year after leaving the hospital, from "cerebrospinal meningitis." Her physician stated that she did not then give signs of hyperthyroidism.

The fourth case had both superior thyroids ligated in March, 1917. No further operation was done at that time. She was then extremely toxic. She existed for several years in a condition of invalidism, going from one hospital to another, having long treatments of *x*-rays, etc. In February, 1924, an effort at operation was made in another hospital and she died immediately following the operation.

It should be noted that ligation of the superior thyroid arteries was successfully accomplished for 3 of these patients, and that they then either would not or could not have further surgical procedure and that the disease progressed in each instance. The fourth died of disease apparently not associated with her goiter.

Division 3. *Patients of the invalid class.* I find only 1 patient in this group. He, too, refused further operation after his superior thyroid arteries had been successfully ligated. He is a man of twenty-six, who was first seen six years ago, having then had his goiter for three years. He had exophthalmus, tremor, weakness, extreme "nervousness," sweating and rapid pulse. Both superior thyroid arteries were ligated. Improvement followed, but he refused further operation. He tried to work as a clerk, but was unable to continue. In February, 1920, the right inferior thyroid artery was ligated by another surgeon. He then made another unsuccessful effort at light work. He was in another hospital for six weeks in 1921. He was seen in February, 1922, and was then weak and suffering from sweating, dilated heart, palpitation and tremor, and his neck was 16½ in. in circumference. He was then three months in another hospital, had twelve *x*-ray treatments, and improvement followed.

He then tried again to do clerical work, but when seen by his physician, March, 1924, had been unable to continue even light work. It is hardly fair to consider him a case of operation. He let his opportunity pass when he refused partial thyroidectomy after his preliminary ligations.

Division 4. *Patients who are able to do a moderate amount of work and enjoy life, but have to guard against overexertion.* There were 32 patients in this group. They were all definitely better than before their operations. Several of them were better than we could fairly expect. Three cases may be cited for illustration, although others in the group were much stronger than were these. A woman of thirty showed marked invalidism from the ordinary symptoms of toxic goiter. After subtotal thyroidectomy and a period of rest in the hospital she regained her health and seemed to be normal for nearly four years. She then suffered from a post-partum hemorrhage. During the following two years her strength was only moderate, but she was able to carry on the ordinary duties of life. Another patient, twenty-eight years old, with severe Graves' disease, had her superior thyroid arteries ligated separately under local anesthesia in 1912, with an interval of seven days between the two ligations. This was followed four months later by hemithyroidectomy. During the following six years she was not able to do much. During this period her disability was increased by family sorrow. She then gained strength, and during the intervening years was able to support herself and help care for her mother.

Another patient, forty years old, made an excellent recovery and was able to return to usual family and social activities. There followed a period of stress owing to misfortune in the family and a corresponding period of depression and limitation of capabilities. Now for three years she has been reasonably active and carefree.

These cases represent the least capable part of the group. Without the operation, most of them, I believe, would have collapsed under their trials or would have been useless invalids.

Division 5. *The group of patients who really enjoy life and have at least the average capacity for work or other activities.*

This is by far the largest group, representing, as before stated, 73 per cent of the patients who were traced after leaving the hospital, or 68 per cent of the entire series, including untraced and fatal cases. Many of them have much more than the average capacity for exertion. For instance, Case 94 announced that "before operation" she could not climb stairs or raise her arm high without distress or "do much of anything," but that now, at the age of forty-nine, five years after operation, she can do more than she had ever been able to do before, attending to her own housework and taking part in various activities. Case 59 reported, eight years after her operation, that she is caring for four children and husband, a big house and garden, and stated with much pride that on the day before she had washed twenty-two windows. Her goiter was large and contained an unusual combination of soft cellular and firm fibrous material.

Case 58 has carried on a life of unusual intellectual activity as a writer during the eight years which have elapsed since her operation, although she has suffered from a broken hip with its necessary confinement during that period. Her operation was for cystic adenoma of fifteen years' duration and two years' rapid growth. At the time of her operation her pulse was 120 and she suffered from palpitation, tremor and perspiration.

Case 12, fifteen years after an operation, "tends store all day, beginning at 6.30 A.M., and does the housework for herself and mother before and after these duties." Her operation was for a very large adenoma of fifteen years' duration and two years' rapid growth, severe pressure symptoms and moderate constitutional disturbance.

These facts are given in detail in an effort to show to others the impression which we have received on studying these patients. This group has impressed the writer as showing more than the average degree of good health and capability. All of them were incapacitated before operation—most of them from "toxic" symptoms—a few from pressure symptoms. Their study indicates a remarkable average of good health after previous disabilities which had been disturbing in a high degree.

It should be stated that in no instance has operation been done for the simple goiter of adolescence or for any other form of simple goiter which did not give definitely disturbing symptoms.

Of late much attention has been given to the query as to how patients with goiter will do without operation or even without treatment.

The histories of some of the patients mentioned in Groups 1, 2, and 3 indicate the condition to which such patients may drift. Two other experiences which throw light on the subject also come to mind. One, a woman of fifty-eight, who had had a goiter for thirty years. Her pulse had frequently been rapid and she had frequently been obliged to stop her labors at housework, but she would always resume them again as soon as the acute attack had passed away. When I saw her she had acute pain in the epigastrium. Her heart was dilated, very irregular and gave beats from 160 to 180 per minute. It was of extremely poor quality and made any operative procedure out of the question. She was very thin and had a large goiter most marked on the right side of her neck and apparently cystic there. This was an example of chronic goiter which had finally resulted in cardiac failure. She died on the following day. The other, a man of forty years, who had lived in the Middle West and had been suffering from the symptoms of acute thyroid disease for three months. He had lost 20 pounds, was weak and had to give up work. He had a severe tremor and rapid pulse and was very nervous. His goiter was soft and of moderate size. He was taken to the hospital for a more thorough examination, but became restless after two days and returned home. His weakness then increased and he died within a few days. All surgeons who see many goiters have similar experiences and are forcibly impressed with the seriousness of the disease in both its chronic and acute forms.

When such cases are contrasted with the results which have followed the operations in this group, one must feel like attacking the disease in a radical manner.

Cancer or Suspected Cancer. The pathology of the thyroid is complex. It brings puzzling problems to both pathologists and clinicians. The most remarkable instance in this group

occurred in a man of forty-eight, who for a year had suffered from a left-sided goiter, with both constitutional and pressure symptoms. An encapsulated cystic tumor $9 \times 7 \times 5$ cms. in its diameters was enucleated from the left lobe of the thyroid. None of the adjoining tissue was removed. Since there was no apparent extension of the growth beyond its capsule and since its enucleation was easy, malignancy was not clinically thought of. However, three well-known pathologists agree in the diagnosis of "adenocarcinoma, probably of low malignancy." At the present time, three and one-fourth years after the operation, the patient is free from recurrence and is enjoying excellent health. Another patient who had a papillary cyst adenoma has now been followed for nine years. He is entirely free from symptoms and is actively engaged in business. He had rapid recurrences after his first partial operations and finally every discoverable bit of thyroid gland was removed and radium was left in the wound for a few hours, in the endeavor to control any fragment which might possibly remain. There was also much pathological and clinical consultation about this case and bad prognoses were generally given. There were two other papillary cyst adenomas in the group, but there was no recurrence or suggestion of malignancy in either of them. Another tumor which clinically suggested a progressing neoplasm was reported "lymphogranuloma of thyroid." The patient made an excellent recovery after its removal, and now in her fifth postoperative year shows no suggestion of recurrence. These cases are mentioned to show the uncertainties of thyroid pathology.

The Relationship of the X-ray to the Thyroid Gland should also be considered. A number of cases here recorded had received *x*-ray treatment before coming for surgery. It is not now possible to say how many. Some of the cases mentioned in Divisions 2 and 3, also received *x*-ray treatment after leaving the hospital. I have treated at least 4 patients by *x*-rays without operation. Two of them were very mild cases and have done well. A third case was toxic; when first treated had a marked tremor, basal metabolism plus 35, with a very small thyroid. He did well under *x*-rays. Another one with a large adenoma and very mild toxic symptoms preferred

x-ray treatment to operation and now after the lapse of a year is in about the same condition as when first seen.

It is notable that experienced roentgenologists consider hyperplastic thyroids the most suitable type for *x*-ray treatment, and that many failures of relief come after *x*-ray treatment of such goiters; also it is notable that adenomata which are not so well suited for *x*-ray treatment produce some of the most disturbing symptoms and respond particularly well to surgery.

The Results of Ligation of the Thyroid Arteries have been interesting. Preliminary ligation of the superior poles of the thyroid gland, including the arteries, has been a common procedure in patients too ill for more extensive primary operation. Definite improvement almost always follows this procedure, so that after two or three months a suitable portion of the gland may be removed. These patients, however, are not always easily controlled and sometimes cannot be persuaded to submit to the secondary operation. Cases already quoted in Groups 1 and 2 show the unfortunate condition into which such patients may drift. One patient, however, did so well after double superior pole ligation that secondary operation was not advised; and now, after the lapse of eleven years, is in excellent condition. She was a young woman of twenty-four with a short history of acute hyperthyroidism.

There are two notable results following quadruple ligation: one, a patient of thirty-eight years, had severe toxic symptoms of five months' duration. She had a rather large symmetrical goiter, exophthalmus, tremor, pulse 120 to 150, and was too weak to work. The superior arteries were ligated in June, 1919, and the inferior arteries in February, 1920—she made a remarkable recovery and has now been working successfully as laundress for more than three years. Another young woman whose symptoms were complex, but who had exophthalmus—moderate-sized goiter, rapid pulse, "nervousness," inability to work and basal metabolism plus 17, recovered her poise after quadruple ligation and at the present time, three years after her first ligation, is successfully conducting a boarding house.

Operation on Patients under the Age of Twenty-one is not often desirable. The goiter of adolescence frequently subsides

without operation. There are two rare exceptions to this rule: first, the young patient who develops extremely toxic symptoms—"true exophthalmic goiter"; second, the young person who develops an adenoma so large as to give pressure symptoms or real disfigurement. An instance of the latter condition may be referred to. Case 16 came to me in 1909 when twenty years of age, having a goiter which had been present twelve years. It was very large and was giving great disfigurement and some pressure symptoms. I removed a large part of it and found it to be an adenoma with cystic formation in some parts. On seeing her fourteen years later, I find her in excellent health. She has had seven children in the meantime and her goiter has returned. Her neck is now the site of a large cystic goiter, similar to the one which was removed fourteen years ago. However, it is soft and does not give pressure symptoms.

There have been a few other adenomas in young girls, which have developed to considerable size and have given definite pressure symptoms. These have been removed with good results.

The Seriousness of Long-persisting Adenomas and the favorable result of operation may be illustrated by the following case: A patient of forty-five years, with a moderate-sized goiter, came to the hospital with a six-year history of disability, having had remissions and exacerbations, but having endeavored to carry on her ordinary duties during most of the period. She has recently shown lack of strength, tachycardia, tremor, nervousness and perspiration, and was unable to work. On admission to the hosptial her disability was extreme. Perspiration, weakness and nervousness were excessive. Basal metabolism was +83. She manifestly was not in condition for surgical procedure. She went to an endowed room in the medical division for five weeks where Doctor Sumner kindly attended to her treatment. She showed considerable improvement, her basal metabolism went down to +30 and then went to +40. Her heart was dilated and rapid and irregular, pulse being 110 to 120. She gave definite evidence of degeneration of the cardiac muscle. However, since the thyroid nodule was apparently encapsulated and since she had ceased to improve under medical

treatment, I removed the nodule by a very short operation and she made a remarkably satisfactory recovery, pulse coming down to 64, basal metabolism reaching normal and her entire mental attitude being satisfactory. Her strength improved and she was able to return to her ordinary duties.

Recurrences. In one instance (just referred to) there has been a recurrence of an adenoma which has reached a large size. In seven other instances there have been moderate recurrences of adenomas, none of them serious.

Hypothyroidism has not been observed in any of the patients.

SUMMARY

1. The results of treatment on these 150 patients may be tabulated as follows:

	Number of patients	Percentage of those patients who were traced after leaving hospital	Percentage of entire group
(*a*) Enjoying good health and able to do at least the ordinary amount of work	103	73.6	68.66
(*b*) Able to enjoy life and do moderate work but carefully avoiding overexertion	32	22.8	21.33
(*c*) Persistent invalidism	1	0.7	.66
(*d*) Died since leaving hospital	4	2.9	2.66
(*e*) Died in hospital	5	....	3.33
(*f*) Not traced	5	....	3.33
Total	150		

2. The operations have been adjusted to meet the strength of the patient, sometimes beginning with the ligation of a single thyroid artery and progressing in stages to the removal of three-quarters or more of the enlarged gland.

3. Acute hyperplastic thyroids have given the most severe symptoms but toxic adenomas have sometimes been almost as serious.

4. Adenomas and so-called colloid goiters have sometimes given distressing symptoms from pressure and unsightliness.

5. Some patients have improved under rest and medicinal treatment and the use of the *x*-ray, but so many failures have been noted in these forms of treatment that operation is believed to be the best form of treatment for a very large proportion of patients with goiter.

6. The pathology of cancer and growths which resemble cancer is very complex.

LEAD-PIPE FRACTURE OF THE RADIUS*

KIRBY DWIGHT, M.D.

THIS is the name that we have given to a rather distinctive fracture of the lower one-fifth of the shaft of the radius. It occurs nearly always in the first part of the second decade of life, being rather more often seen in boys than in girls. It is caused by a fall on the palm of the hand just as a Colles' or a fracture of both bones is caused, and usually the force is not great—a simple fall on the ground while playing.

In its pathology, the fracture is essentially a greenstick, but a very moderate one. There is a bending of the bone to a slight degree; and this is not a simple bending as is sometimes found in the very young, nor is it accompanied by separation of the bone substance on the outer side of the curve as is the case in the ordinary type of greenstick fracture: there is simply a wrinkling of the cortex on the inner side of the curve, usually just one deep wrinkle, together with a slight flattening of the bone and a little widening of it just at this point. The similarity to the condition caused by giving a piece of thin-walled lead pipe a sharp bend is very marked. The only place where there can be found any sign of a break in continuity of bone substance is on the edges where the broadening is greatest, and here it is very slight—just enough to enable one to be certain that the alteration in shape of the bone is a recent and not an old occurrence.

The symptoms are not marked. There is some pain and aching in the wrist, and some loss of function due to the pain; there is slight swelling, rarely any ecchymosis, and there is so little deformity that it is easily obscured by an equally small amount of swelling; when seen it consists in an angulation moderate in degree with the apex of the angle directed forward. The most definite symptom, however, and the one

* This paper was written especially for The Roosevelt Hospital Report, 1924.

upon which the diagnosis is usually made, is the perfectly definite *line* of tenderness extending around the radius on all the three sides that can be palpated. There is, as a rule, no indirect tenderness, or bony irregularity; there is no false point of motion, no crepitus and no appreciable shortening.

The roentgenogram must be a good one to show the fracture, for the angulation is slight; but with a clear film the

Fig. 20.

angulation, the wrinkling and the broadening are easily seen and the nature of the injury is manifest.

The diagnosis is easy even without the *x*-ray, the line of tenderness being enough to establish it. It is differentiated from a Colles' or a separation of the epiphysis without displacement by the higher level of the line of tenderness; and from a fracture of both bones by the lack of false point of motion; or if a greenstick, by the lack of tenderness over the ulna and by the lesser degree of angulation. It is most likely to be confused with a simple contusion or sprain, however,

and here the line of tenderness must be sought for and mapped out in order to avoid error.

The treatment is simple immobilization for a few days until the pain has gone. This is followed by mobilization and massage.

The prognosis is very good. The pain and disability disappear after a few days and the function of the forearm and wrist soon returns to normal. There is left a slight angular deformity, but it is soon outgrown.

TRAUMATIC OSTEOMYELITIS*

KIRBY DWIGHT, M.D.

TRAUMATIC osteomyelitis means, in the great majority of cases, infected compound fractures, and its interest at the present time lies in the great advance in its treatment made possible by the immense number of such cases occurring during the war.

We can all remember the extreme chronicity of the cases of infected bone with sinus formation that we have had to do with in our hospital work. We can remember old cases with sinus that had been under treatment for years. That was the state of our knowledge of this condition at the beginning of the late war, and it was not until two years or more had passed that any great improvement was made. By that time there were hospitals and hospital camps filled with these chronic cases, and hope of curing them in time to be of further use in the army had about been given up.

It was my good fortune, on returning to the United States, a year ago, to be assigned to a reconstruction hospital where I remained for several months in charge of the osteomyelitis work. It was extremely interesting to see and in some measure to learn the new forms of treatment, and to note the comparative rapidity with which real cures were effected.

The cases at Colonia were of course mainly compound fractures, the result of shell or gun-shot wounds. In civil life we see similar conditions resulting from ordinary compound fractures or from other injury to bone which lays it open to infection, such as infection following operation on bone or a hematogenous infection following simple fracture.

The essence of these cases is that the infection gains entrance into a bone that has just been broken or chiselled into, and that it starts at the point of injury. Consequently

* Read before The Roosevelt Hospital Alumni Association in February 1920.

the inflammation remains more or less definitely localized in this vicinity and does not travel long distances up and down, for the break in the continuity of the bone has already established drainage, at least into the soft parts, and the infection is not forced along the marrow cavity.

Of the *pathology* in the early stages there is little to be said. There is the injury to the bone, more or less necrosis, the formation of callus and the inflammation of the soft parts.

In the late stage the fracture has, as a rule, united, there are sequestra present, often multiple, and this sequestration may be the result of the splintering of the bone as well as of the infection. There is considerable callus formation unevenly distributed around the bone, and this callus is perforated by one or more sinuses that lead to the sequestra inside, or to a cavity. Sometimes these sinuses pass through the crevasse of one of the original lines of fracture. In a considerable number of cases there are no sequestra and the sinus leads merely to a cavity in the bone or to a hole through the bone. These are usually cases in which an incomplete operation has been done previously, the operator having been content to remove sequestra and other dead bone and to provide drainage. Here the failure to heal seems to be the result of mechanical conditions rather than of infection, for even if these cavities are sterilized they usually fail to heal. The trouble is two-fold: in the first place bone seems to be unable to support a luxuriant growth of healthy granulation tissue; in the second place there is the problem of the rigid-walled cavity, like that of a chronic empyema. The walls cannot collapse to obliterate the cavity and the bone is unable to fill it with healthy scar tissue.

The *symptoms* in the early stages are simply those of the fracture plus those of an infection particularly manifest in the soft parts. In the late stage the fracture has united, as a rule, and there are no signs of inflammation in the soft parts unless there is deficiency in drainage. But there is an enlargement of the bone at the site of trouble. There will be found a sinus or sinuses leading down to or into the bone, and the exploring probe may detect bare bone, loose bone, or merely a cavity in, or a hole through, the bone. These sinuses may close over at times, only to break open again.

The discharge may vary both in quantity and character. Usually it is yellow pus, but it is sometimes rather thin; and when a joint or bursal sack communicates with the sinus, it shows the characteristics of synovial fluid. There may be great variations in the quantity of discharge, and this is an important diagnostic point, as it varies directly with the amount of necrotic bone or the size of the bone cavity.

The *x*-ray is an indispensable aid to diagnosis, showing the presence of sequestra, the size and shape of cavities in the bone and the amount and character, as well as the location of the union between the two main fragments. It is, however, sometimes difficult to read. It is hard to distinguish all the sequestra which may be present, owing to the amount and irregular composition of the callus and other new-formed bone, the small size of some of the sequestra and the occasional presence of splinters of living bone which may simulate them. It is interesting to note in this connection that the sequestra are of greater density to the *x*-ray than the living bone. The reason for this is that the living bone undergoes a process of osteoporosis and becomes permeable to the ray, while the dead piece, being cut off from all the vital processes, retains its original density.

In respect to the amount and character of the union present it is often difficult to differentiate between the bony and the fibrous unions which may exist at the same time in different parts of the same fracture. A stereoscopic *x*-ray is of great aid in determining this important point. For without it, and occasionally even with it, this differentiation may only be made during the course of the operation, when, in chiselling away bone to get access to the sequestrum or the cavity, one by chance takes away that part which has bony union, and leaves intact only that part which has fibrous union. A moderate amount of false motion is at once evident. Fortunately no great damage is done in this case, as union takes place again quite readily, but it adds to the amount of work in the after-care.

As to the constitutional symptoms, there are none when the drainage is adequate, except in those cases where the discharge is very profuse. Here there may be a gradual deterioration in the general health.

TREATMENT

The treatment may be divided into four classes, depending on four periods in the disease. The first period is the pre-infective one, and in civil life it is perhaps the most important one as regards treatment. In this period, which lasts on the average about twelve hours, operative measures should be taken to prevent infection. The old methods of liberal incisions to provide drainage and the free use of antiseptics are now reserved for the later stages if they arrive. The early treatment should be to prevent, not to minimize infection. In the operating room, with a general anesthetic, and under the best possible conditions, a careful debridement should be done. And *following* the debridement, the fracture should be reduced and the wound sewed up tight, a plastic repair being made if necessary to close the wound. If infection does supervene in spite of your efforts, or if the patient arrives with infection already established, then the treatment for the second or infective stage is indicated. It is, in the main, drainage.

In the third stage one's efforts are directed toward obtaining union of the fracture in good position, and toward promoting healing by maintaining drainage, removing fragments of dead bone and by the use of the Carrel-Dakin treatment. Healing may take place during this stage. If it does not, the condition gradually passes into the fourth or chronic stage, whose symptoms and pathology have been noted above.

In this stage the treatment may be expectant or operative. The expectant treatment is used in those cases where the amount of discharge is small, where there are no sequestra evident, or at most one or two very small ones, where there is no large hole through or cavity in the bone and when there is in each case progressive improvement. If the condition remains stationary for several months, no matter how slight the symptoms may be, an operation is indicated.

Another class of cases in which expectant treatment may be used is that in which the union of the fragments is of recent date, and where the *x*-ray shows that the amount of union is slight, union at but one small point in the line of

fracture, a union that would be jeopardized by operative interference. In these cases it is often advisable to postpone the operation for several weeks in order that the union may become stronger and more extensive.

The *operative* treatment consists in the laying-bare of the bone, the removal of sequestra and other necrotic material, and the shaping of the cavity in the bone to provide for postoperative treatment and to favor healing.

The incision is a fairly large one, longitudinal rather than transverse, either over the sinus, excising the scar, or on some other aspect of the limb more suitable anatomically for a large incision. For example, in the humerus the sinus may be on the inner side of the arm, in close proximity to the brachial vessels and the median and ulna nerves. In this case it is often better to make the incision on the outer side, where only the musculospiral in the lower part, or the circumflex in the upper, will have to be avoided. Over the tibia it is better to make a curved incision with the convexity outward, so that the resulting scar may not lie in immediate juxtaposition to the bone.

The incision having been made and deepened down to the bone, the periosteum is split longitudinally with the knife and carefully stripped back from the bone, taking care to keep close to the bone in so doing, so as to preserve as much as possible of the osteogenetic layer of the periosteum. Then the bone is carefully examined to see how the sinus runs into it, and if possible the extent and the location of the bony union between the fragments. These things determine our approach into the bone itself, our aim being to remove bone that can best be spared and to leave intact sufficient bony continuity to prevent a refracture.

The point of attack having been determined, usually to one side or the other of the opening in the bone, with mallet and chisel enough bone is cut away to give access to the cavity within. This cavity is then explored and all sequestra removed, care being taken not to break them, especially the long slender ones that may extend for an inch or so up or down within the bone, and that may require additional chiselling before being removed. Then the granulation tissue is curetted away and we are ready for the shaping of the cavity.

Experience has taught us that the simple removal of the sequestra is not enough, at least when they lie within the bone in a cavity of any size; for neither can the postoperative treatment to prevent reinfection be carried out, nor can the soft parts be utilized to obliterate the cavity. The cavity must be thoroughly opened up through all its clefts and pockets, new sequestra of small size often being found in so doing. Then the margins of the cavity must be cut away so that its walls are not overhanging or even precipitous, but sloping so that there is easy access to the entire cavity for the Dakin's tubes which are used in the after-treatment.

If possible the walls should be made even more sloping than this, so sloping and sloping in such a way and in such a direction that the adjacent soft parts can easily be pressed into the cavity, completely filling it. These soft parts are not held in this position, for that would prevent the adequate use of the Carrel-Dakin after-treatment, but they will subsequently, with or without a secondary operation, collapse or be pressed into the cavity, completely obliterating it. This is the ideal, but it is not always possible of fulfilment, sometimes because the cavity is too near the extremity of the bone, in the cancellous tissue, sometimes because of the danger of refracture, when the amount of union is slight and the removal of a large part of the connecting bridge would be necessary. In the former case, a flap may be made of some of the neighboring soft parts, preferably muscle, arranged so that it will swing into the cavity; or at a later period, when sterilization has been effected, this muscle flap or a free-fat graft may be made and the wound closed. In the latter case a muscle flap may be used; or a later operation may be performed at a time when there has been enough new bone formation to allow of the ideal shaping of the cavity.

The treatment for those bone cavities which contain no sequestra is similar to the preceding, and the same principles hold good in the treatment of that pathological condition which consists in a hole extending entirely through the bone with a persistent sinus accompanying it. The procedure here is to take away all the bone on one or the other side of this tunnel so that there is no longer any hole, and then to

shape the sides of this channel, as has been outlined above, so that the soft parts may collapse into the space.

As a final step in these operations it is well to incise the periosteum longitudinally in several places, so that additional blood supply may be obtained from the overlying muscles to nourish the granulation tissue which will cover the bone.

Dakin's tubes are then placed in position, or, if there is still considerable oozing, as there often is, especially when a tourniquet has been used, the wound is packed open and the tubes are inserted at the first dressing.

The after-treatment consists in the use of Dakin's solution; and if this treatment is perfectly carried out and the operation was properly done, it should be possible after a short lapse of time to do a secondary closure with good prospects of success. Even in cases where the secondary closure is unsuccessful or was not attempted, the wound often heals up giving a permanent cure; if not, the cause is usually an insufficient operation, and after an interval of from six weeks to two months one must try again.

A LARGE MYCOTIC EMBOLIC ARTERIOVENOUS ANEURYSM OF THE FEMORAL VESSELS*

ROLFE FLOYD, M.D.

THIS case is reported because of the large size of the sac, its large venous connection, the fact that, without rupture, it caused initial and pronounced symptoms before the underlying viridans endocarditis was evident, and finally because there was septic endarteritis with a thrombus in the opposite femoral artery establishing the mycotic embolic origin of the aneurysm.

The historical steps in the recognition of mycotic embolic aneurysms are somewhat as follows:

First, embolic abscesses of artery walls were recognized in 1844 by Rokitansky.[1] Then in 1853 Tufnell[2] definitely recognized the dependence of an aneurysm on emboli derived from vegetations on the heart valves.

Twenty years later Ponfick[3] in 1873, published 7 cases and expressed new views about the pathogenesis of the condition. He recognized that the causative endocarditis was regularly acute, usually an acute engrafted on a chronic process, that the aneurysms were usually small, multiple, and frequently found in cerebral or abdominal vessels, that they belonged to adolescence and early adult life and occurred in arteries otherwise normal. He further believed that the damage to the artery wall began on the side next the lumen and worked out, and that thus the intima, elastica, and media were usually broken through and the sac wall was composed of adventitia and new-formed layers, either organized thrombus inside or inflammatory tissue outside. He also observed that these lesions usually developed at or just central to points where the arteries divide. All these observations and conclusions have been confirmed by the work of later students on the subject.

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Ponfick also believed that the loose areolar tissue of pia and peritoneum offered no accessory support to a weakened arterial wall and so negatively favored its distention, a factor which seems real but not entirely determinant, for these lesions also occur in the comparatively dense tissues of the extremities.

By a peculiar freak of circumstance in one of his first cases, he found a sharp calcified embolus that had pierced the entire artery wall, a lesion apparently of the utmost rarity. This experience led him to consider the production of all embolic aneurysm to be mechanical; he searched assiduously for a minute particle of lime in every case, and when he could not find one he believed the erosion of the vessel wall to be due to mechanical pressure of the embolus against the wall, made more effective by the pulsating pressure of the blood stream, a "decubital necrosis" analogous to bedsore formation. He accordingly denied the primary chemical action and infectious nature of cardiac emboli though fully appreciating these qualities in emboli derived from infectious venous thrombi. This mechanical pathogenesis has not been generally accepted, although 2 cases similar to Ponfick's unquestionable one were reported by Thoma[4] in 1889.

In 1887, fourteen years later, Eppinger[5] made an exhaustive study of the subject and, except in one point, his views, added to the accepted ones of Ponfick, form the basis of the present conception of the condition.

In the first place he showed that the same bacteria were present in the fresh cardiac vegetations and in the emboli, and concluded, in contrast to Ponfick's mechanical theory, that the damage to the artery wall was due to inflammatory and destructive changes induced by these bacteria. He accordingly introduced the term *mycotisch embolishe.*

He especially emphasized the rupture of intima and elastica, demonstrated their torn edges at the sac mouth and considered the rupture of the elastica as a constant feature and a prerequisite in the pathogenesis of the lesion. The media he found usually ruptured but sometimes partly preserved in the sac wall, and the adventitia its only constant component. In recent cases he found the infectious embolus and active septic inflammation of the vessel wall, but in cases of longer

standing, where these features were no longer demonstrable, he considered the ruptured edge of the elastica at the sac margin diagnostic and multiplicity of the lesion an added confirmation.

He, however, held a peculiar notion about the way the lesion developed in the vessel wall, namely, that the first step was the development of a septic periarteritis in the tissue just outside the vessel opposite the site of lodgment of the embolus, the second step a septic mesarteritis which finally burst into the lumen, like an abscess, first undermining and then rupturing the elastica and intima in the process.

This view has not found general acceptance, and its opponents believe that Eppinger was led astray, just as Ponfick was, by encountering a very rare condition in one of his cases, namely a septic embolus of one of the vasa vasorum, and interpreting his other cases on this basis.

Those who oppose Eppinger's view hold that the inflammation begins in the artery wall where the thrombus lies in contact with it and progresses from the lumen outward.

Unger,[6] in 1911, wrote an excellent and convincing paper with careful microscopic studies establishing the correctness of this conception. In one of his cases with septic endocarditis there was no aneurysm but an ulcerative lesion in the femoral artery just where the profunda comes off, septic inflammation of the vessel wall, local destruction of the intima, elastica, and part of the media, and a septic thrombus adherent to the ulcer partly occluding the lumen of the vessel. This is almost exactly the lesion which the case I report showed in the left femoral artery.

Aneurysms can occur with acute endocarditis in another way. Vegetations may form on the aortic wall, especially in the ascending aorta, just as they form on the valves or on the mural endocardium and the vessel wall beneath them may be ulcerated, weakened, and may pouch into sacculated aneurysms which are mycotic but not embolic. Such are reported by Osler,[7] 1885, and McCrae,[8] 1905.

Lewis and Schrager,[9] 1909, in an excellent review of the subject preliminary to reporting their own cases, state that "the case reported by Osler in which one of the aneurysms

was as large as a billiard ball is probably the largest embolomycotic aneurysm observed." Unger, 1911, however, reports one of the left femoral artery 11 by 10 by 7 cm., the largest of which I have been able to find a previous record. The one I am about to describe measured 15 cm. in length and over 6 cm. in diameter.

Unger, reviewing the reported cases in 1911, found 91 mycotic-embolic aneurysms of which 8, or nearly 9 per cent, were femoral and situated at the point where the profunda femoris comes off.

Arteriovenous aneurysm, on the other hand, appears in the literature as a comparative rarity up to the onset of the late war in 1914, since which many have been reported. Practically all such cases are regarded as due to the simultaneous penetration of an artery and vein where they lie close together by a weapon or projectile. I have, however, found only 2 cases of embolic-mycotic arteriovenous aneurysm described; one by Simmonds,[10] 1904, the second by Libman,[11] 1907.

Simmonds' was a sacculated aneurysm the size of a hen's egg, at the aortic bifurcation, which secondarily perforated the right common iliac vein by a hole the size of a lead pencil. It occurred in a woman thirty-one years old dying of puerperal sepsis without giving pronounced symptoms of the aneurysm.

Libman's case was in a man, twenty-five years old, sick of infectious endocarditis who suffered with pain in the groin for four weeks and then developed an elastic swelling in the left femoral region, painful and tender, with expansile pulsation and a loud systolic diastolic humming murmur with a systolic accentuation. The "left femoral artery showed quite marked endarteritic changes. There was an aneurysm at the point where the profunda was given off. The sac contained thrombotic masses, most of which were not at all decolorized. The remains of the vessel wall were present in the sac. The femoral vein had a small deficit in its wall externally and anteriorly which led into the sac." Staphylococcus aureus was found in the sac and streptococcus and staphylococcus aureus in the heart blood. The ordinary aneurysm of later life, usually developed in syphilitic vessels, may, however, perforate into a vein, and so produce an arter-

iovenous aneurysm. Such a case came under my care on the 2d Medical Division at Bellevue Hospital in January, 1916. A man with an enormous sacculated aneurysm of the ascending aorta was profoundly cyanotic for two weeks before death and at autopsy there was found a slit-like opening about 1 inch long from the superior vena cava into the sac.

Following is the record of the case which it is the purpose of this paper to report:

Carpenter, age 36; admitted to Roosevelt Hospital, July 31, 1919, complaining of rheumatism. Five of his brothers have rheumatism, but he had never had it before. He himself had measles, diphtheria, mumps, whooping-cough, and frequent sore throat, as a boy. He is subject to attacks of indigestion and vomiting. He has had a right hydrocele for seven years which has been repeatedly tapped. Otherwise his health has been good. No cardiac or renal symptoms. There is no history of any injury or wound in the right leg or groin. Ten weeks ago he noticed his right ankle was swollen but not painful. A little later he began to have pain all through the leg, which was worse when the leg was kept quiet, and was relieved by massage. Both the swelling and pain have increased up to the time of admission.

Examination. Color and nutrition about normal but he has the face of pain. No pharyngitis; pupils react normally. Lungs are normal. Heart is slightly enlarged, action regular but a little too strong, 100; soft systolic murmur at the apex, transmitted to the axilla. Abdomen is normal; neither the liver nor the spleen is enlarged. There is marked pitting edema of the whole right leg and right side of the scrotum. There is no evidence of inflammation of the knee or ankle, but motion, especially extension, of the hip causes much pain. There is a large hard pulsating tumor just below Poupart's ligament, over which a distinct systolic thrill is felt, and a systolic and diastolic murmur heard. The tumor is quite tender on pressure. No tumor or pulsation is felt above Poupart's ligament, but there is tenderness in this region. There is no edema elsewhere. Rectal examination is negative. Urine on repeated examinations regularly showed a trace of albumin, never any sugar, rarely a few casts. *X*-ray showed nothing abnormal in the chest or in the right hip-joint. Blood cultures at first were sterile but at the end of two weeks showed streptococcus viridans, a finding which was confirmed by subsequent examinations. Wassermann test on the blood was negative. Blood examinations made on admission and later resulted as follows:

Hemoglobin, per cent	White cells	Polymorphonuclears, per cent
60	11,800	70
80	8,600	72
85	7,600	68

He ran an ordinary septic temperature, usually between 99.5° and 102.5° and never reaching 104°. The pulse was rapid in proportion to the temperature,

almost always over 100 and averaging about 110. The respiration ran between 20 and 24.

Although I made the diagnosis of aneurysm, probably arteriovenous, on admission, much doubt about the case developed later because it hurt him too much to extend the thigh, and in semiflexion, and with the general edema and local inflammation about the sac, it was hard to be clear about the nature of the tumor and, much of the time, impossible to get any pulsation in it. Added to this came the fact that the diastolic murmur was absent most of the time and the systolic a good part of it. As a result the diagnosis of septic thrombosis of the external iliac vein had more advocates than had aneurysm when he died on October 21, eleven weeks after coming to the hospital, and five months after the appearance of his initial symptoms of swelling of the right leg. The cardiac condition had meantime become increasingly evident, not only from the cultures, but from cardiac symptoms and conjunctival and cutaneous petechiae as well.

The autopsy which I performed about eighteen hours after death showed: acute endocarditis of mitral and aortic valves; arteriovenous aneurysm of right femoral vessels; septic arteritis of left femoral artery; acute exudative nephritis with tubal hemorrhages and infarcts; enlarged spleen with infarcts; petechial hemorrhages of skin and conjunctivae; edema and congestion of lungs; double hydrothorax; general subcutaneous edema especially marked in lower trunk and legs, massive in the right leg; old hydrocele.

The heart showed distinct but not extreme enlargement of the cavities of both ventricles with decided thickening of their walls. Valves of the right side were normal. Mitral valve had huge vegetations of yellow fibrin with recent bloody deposits on both cusps, and there was considerable ulceration with loss of substance of the cusp edges. The aortic valve had a fibrin vegetation 3 mm. in diameter and 1 cm. long on one flap which was inflamed and penetrated at the point of attachment of the vegetation; another aortic cusp bore a small recent vegetation, while the third was normal. There was a small mural vegetation on the ventricular endocardium well below the mitral orifice. The muscle wall of the left ventricle was extensively studded with whitish areas which looked like patches of fibrous tissue. Coronary vessels were normal. The pericardium was normal. Under the microscope the heart muscle showed areas of degenerated or absent muscle with a growth of fibrous tissue; pus and round cells infiltrated these areas very irregularly, sometimes practically absent, sometimes quite copious and collected into small foci, but never constituting true abscesses. In two instances a plug of fibrin and pus cells were to be seen inside small vessels penetrating areas of muscle degeneration; in one case the vessel wall was indistinct and evidently damaged. Thus the areas of degeneration seemed to be embolic and the effects of the emboli both mechanical and septic.

The aorta showed only some insignificant patches of ordinary sclerosis.

The kidneys were rather large, with several yellow cortical infarcts; capsules were not adherent; the color a light buff sprinkled with red pin points; cortex of normal relative thickness but its markings obscure; medulla dark red in sharp contrast. Under the microscope small groups of tubes were filled with blood causing the red spots seen in the cortex. The epithelium of the convoluted

tubes was mostly somewhat flattened and the tubular lumina enlarged, but there was no exudate in them except for a very moderate amount of coagulated matter, hardly more than normally seen. The glomeruli showed a general but slight increase of the tuft cells obscuring the outlines of the individual capillary loops to some extent. The straight tubes of the medulla were many of them full of blood, which accounts in large part for its red color. The capillaries both of cortex and medulla were comparatively empty. The connective-tissue stroma was not increased. Some of the smaller arteries were slightly thickened.

There was a large sacculated aneurysm springing from the posterior surface of the right femoral artery in Scarpa's triangle, by an orifice elongated in the axis of the vessel, 2.5 cm. long and about 0.7 cm. wide, with smooth edges. The femoral vein lay on the front wall of the sac and there was an opening from the vein into the sac, also elongated in the axis of the vessel, 5 cm. long. Its edges also were mostly smooth. Thus the openings from artery and vein into the sac lay parallel and side by side, the venous opening having the greater vertical extent. The sac was 15 cm. long and over 6 cm. in diameter. It extended up behind Poupart's ligament into the iliac fossa and the ilium was so deeply eroded beneath it that the acetabulum was opened and the head of the femur lay against the sac. The femur, however, showed no erosion. The sac contained clotted blood but no extensive laminated mural clot. There was a good deal of inflammatory tissue, apparently mostly new connective tissue, about the sac, so that its dissection was somewhat difficult. There was no appearance of hemorrhage with false sac-wall formation or anything to suggest a dissecting aneurysm. The femoral artery showed some sclerosis of the Moenckeberg type with annular depressions of its wall. Unfamiliar with the literature, I failed to look for the torn ends of the intima and elastica at the margins of the sac mouth.

In the left femoral artery just below Poupart's ligament there was an ulcerated area, soft and necrotic, about 3 cm. long, to which a large thrombus was adherent which partially occluded the vessel. This artery, like its fellow also, was the seat of Moenckeberg's sclerosis, a lesion which apparently had nothing to do with either the aneurysm or the thrombosis. Under the microscope the artery wall was found infiltrated with round and pus cells; the intima was completely lost; the membrana elastica could be traced through part of the circumference. Deeper in the wall of the media could be seen the lime deposits of Moenckeberg's sclerosis. The thrombus was large and partly filled the lumen; it was attached to the artery wall in two places. Blood-vessels penetrated it and fibroblasts were growing in it. On one part of it was a fresh deposit of fibrin and leucocytes. There were a number of phagocytes containing brown pigment in the artery wall and clot margins. A section stained with methyline blue showed no microorganisms (Fig. 21).

The unusual features of the case then are: (1) The large size of the sac, its wide venous connection, and the density of its wall, preventing its rupture and enabling it to erode bone. (2) The extensive lesion inside the opposite femoral with ulceration and formation of an organizing thrombus but

without any aneurysmal dilatation. These features appear to depend in part on an infecting organism of low but persistent virulence which allowed time for extensive connective-tissue growth, and in fact may have stimulated it. This low virulence is evidenced by the long duration of the illness, the late appearance of cardiac symptoms, the character of the lesions in the muscle wall of the heart as well as of those in the right and left femoral arteries.

FIG. 21. Femoral artery split open. S-S. Edges of split. L. Lumen. E. Elastica. M. Media. A. Adventitia. T. Thrombus. T_1 and T_2 Attachment of thrombus. MT. Mural thrombi. B. Blood, post mortem.

I have found some 55 references in the literature bearing on the subject, but only those referred to in the paper are listed.

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NON-PROTEIN NITROGEN AND BLOOD PRESSURE IN RELATION TO KIDNEY AND HEART LESIONS*

ROLFE FLOYD, M.D.

THE purpose of this paper is to show certain relationships between non-protein nitrogen and blood pressure on the one hand, and structural changes in the kidney and heart on the other. It is based on 50 cases in which the non-protein nitrogen was determined during life and on which I performed autopsies and examined the organs microscopically. In only two-fifths of these cases was nephritis the chief, or an important, contributory cause of death.

As so often happens in writing up routine hospital cases, the observations are neither so well controlled nor so complete as desirable. Thus the blood pressure and the heart and kidney weights were not always recorded; the blood pressure and non-protein nitrogen observations were taken at varying and sometimes considerable intervals before death; and so on. In spite of these imperfections, the work is presented because more observations on the relation of clinical findings to lesions are essential to the solution of the present kidney problems.

In the kidney, microscopical changes are far more significant than gross ones; so in this study only the following structural alterations are considered:

1. Changes in the combined weight of the two kidneys. The normal figure has been considered to be from 270 to 300 gm. for the adult.
2. The occurrence of an inflammatory exudate in the form of pus cells, red blood cells, coagulated matter and casts as they occur in the lumina of the tubules and of the glomeruli or, less commonly, in the interstices of the stroma. The exudate has been described as (*a*) absent, (*b*) slight, (*c*) marked, and (*d*) very great. It is obvious that such a classification is both ill-

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defined and too dependent on the personal equation, although the latter error is somewhat controlled by a rather wide experience in kidney sections. The same division into four degrees of change is followed in dealing with other kidney and heart lesions.

3. Degeneration of the epithelium of the convoluted tubes consisting of swelling, distortion, granulation, vacuolization and desquamation. (Necrosis did not appear in this series.) These changes are difficult to judge of because post-mortem changes occur early, probably within six hours, and closely simulate those which occur before death. In most kidneys brought to microscopical study, therefore, post-mortem effects are present, and often ante-mortem phenomena in addition. I have recorded the changes as seen, but, except in early autopsies or marked lesions, such observations must be interpreted with reserve.
4. Changes in glomeruli which include an increase in the tuft cells obscuring the capillary loops, matting of the loops, waxy degeneration of the loops, increase of the capsule cells to form crescents, thickening of Bowman's capsule, shrinkage and atrophy of the entire structure with obliteration of the tuft.
5. Increase of connective-tissue stroma, in subcapsular wedges, in irregular patches, or diffusely, varying in relative amounts of cells and of basement substance.
6. Thickening of the arteries, presenting the ordinary or obliterating type of endarteritis.

Structural changes in the heart are considered under four heads:

1. Changes in heart weight. The organ was freed of its contents before weighing.
2. Changes in the heart valves: thickening, distortion, vegetation and destruction.
3. Changes in the heart muscle, consisting of areas of degeneration and necrosis, areas of fibrosis, areas of infiltration with pus or round cells.
4. Thickening of the coronary arteries, similar to the endarteritis seen in the kidney and elsewhere.

THE RELATION OF NON-PROTEIN NITROGEN TO KIDNEY CHANGES

The non-protein nitrogen was found to vary more directly with the amount of stroma in the kidney cortex than with any other renal lesion.

There was almost no relation between non-protein nitrogen figures and changes in the renal epithelium. There was, however, a definite tendency for the non-protein nitrogen and the amount of the exudate to vary together, and the same proved true in regard to glomerular and arterial changes.

In other words, an increase of non-protein nitrogen goes with an increase of the inflammatory exudate in the kidney, an increase of glomerular lesions and an increase of arterial thickening, but its increase corresponds most closely with an increase in the connective tissue while there seems to be very little relation between it and the amount of epithelial degeneration.

The significant relation of kidney weight to non-protein nitrogen was the increase of average non-protein nitrogen in small kidneys, a result to be anticipated since such organs are the ones that show the maximum obliteration of tubules and glomeruli. In the table normal non-protein nitrogen figures occur with high kidney weights, but this result is based on 4 cases, 1 of which had waxy kidneys weighing 660 gm. In 2 others, however, the kidney weights were large, 500 gm. and 380 gm. respectively, but the organs were without other significant abnormality. Whether these large normal kidneys represent a hypertrophy in response to some physiological demand which has resulted in an increase of the normal functional power must be determined by further studies. Such a condition occurs, at any rate, in the heart when first put under continued strain. Also I believe that those who drink large amounts of beer have been observed to have large kidneys without inflammatory changes.

Some of the detailed results are here tabulated to support the above statements and to enable other observers to include them in larger series of observations. In looking at this and subsequent tables the following average figures for the entire series must be constantly kept in mind.

		No. of observations
Average kidney weight	329 gm.	43
Average heart weight	448 gm.	35
Average blood pressure	153 mm.	38
Average N P N	116 mg. in 100 c.c.	50

RELATION OF NON-PROTEIN NITROGEN TO KIDNEY WEIGHT

N P N	Average kidney weight	No. of observations
Up to 30 mg.	460 gm.	4
31–50 mg.	322 gm.	13
51–100 mg.	312 gm.	9
101–200 mg.	321 gm.	8
Over 200 mg.	293 gm.	9

RELATION OF NON-PROTEIN NITROGEN TO INFLAMMATORY EXUDATE IN THE KIDNEY

Exudate	Average N P N	No. of observations
No exudate	44 mg.	12
Slight exudate	98 mg.	13
Marked exudate	167 mg.	17
Very large exudate	145 mg.	8

RELATION OF NON-PROTEIN NITROGEN TO DEGENERATION OF THE RENAL EPITHELIUM

Epithelium	Average N P N	No. of observations
Normal	43 mg.	9
Slight degeneration	132 mg.	18
Marked degeneration	133 mg.	23

RELATION OF NON-PROTEIN NITROGEN TO GLOMERULAR CHANGES

	Average N P N	No. of observations
Glomeruli normal	35 mg.	7
Slight glomerular lesions	92 mg.	14
Marked glomerular lesions	142 mg.	19
Extreme glomerular lesions	158 mg.	10

RELATION OF NON-PROTEIN NITROGEN TO INCREASE OF CONNECTIVE TISSUE IN THE KIDNEY

Stroma	Average N P N	No. of observations
Normal	56 mg.	19
Slight increase	61 mg.	11
Marked increase	191 mg.	9
Extreme increase	215 mg.	11

RELATION OF NON-PROTEIN NITROGEN TO THICKENING OF RENAL ARTERIES

	Average N P N	No. of observations
Normal arteries	80 mg.	22
Slight thickening of arteries	97 mg.	11
Marked thickening of arteries	163 mg.	14
Extreme thickening of arteries	239 mg.	3

At the first glance thickening of the renal arteries seems to correspond to a higher non-protein nitrogen than does stroma increase, but the higher figure, 239 mg., occurring with extreme arterial change is based on only 3 cases. If the cases showing little and no change are compared with those showing marked and extreme change in each series the greater correspondence of non-protein nitrogen with variation in the stroma becomes at once apparent—thus:

	Average N P N	No. of observations
Little or no stroma change	58 mg.	30
Marked or extreme stroma change	240 mg.	20
Little or no arterial thickening	85 mg.	33
Marked or extreme arterial thickening	148 mg.	17

It is interesting in this connection to recall that Delafield, who saw a great many autopsies on cases which had been under his observation during life, defined chronic nephritis as a disease whose essential and characteristic lesion was the growth of new connective tissue in the kidneys, although his work was done without knowledge of the non-protein nitrogen.

Volhard and Fahr likewise found that "glomerulo-nephritis," in which an increase of the stroma is early and important,

was associated with higher non-protein nitrogen figures than either "nephrosis" or "sclerosis" in which the increase of stroma is less pronounced and of later development.

The reason for this elevation of non-protein nitrogen figures as the stroma increases is, I believe, the corresponding absence or deterioration of tubes and glomeruli. Whether the increase of connective tissue is looked at as the primary fact in the inflammation or as a replacement fibrosis secondary to primary destruction of the secretory structures, the ultimate result is the same. A kidney section that shows a lot of connective tissue must contain comparatively fewer secretory elements. If the whole organ were over-size due to an increase of connective tissue without any concurrent destruction of the tubes and glomeruli, then the above view would not hold, but I have never seen such an organ showing no damage to the secretory elements.

RELATION OF NON-PROTEIN NITROGEN TO HEART LESIONS

The heart weight shows a definite tendency to increase with the non-protein nitrogen, probably incident to the rise of blood pressure that, as a rule, occurs with increasing nitrogen in the blood.

On the other hand, no definite relationship was found between various lesions of the valves, myocardium and coronary vessels and variations in non-protein figures. The tabulated results follow:

RELATION OF HEART WEIGHT TO NON-PROTEIN NITROGEN

N P N	Average heart weight	No. of observations
Up to 30 mg.	268 gm.	3
31–50 mg.	427 gm.	12
51–100 mg.	473 gm.	4
101–200 mg.	472 gm.	8
201 mg. and over	503 gm.	8

This relation of heart weight to non-protein nitrogen is not a vital one, for it fails to come out when the table is reversed so as to show the average non-protein nitrogen that occurs with progressively increasing groups of heart weights.

RELATION OF NON-PROTEIN NITROGEN TO HEART WEIGHT

Heart weight	Average N P N	No. of observations
Up to 300 gm.	49 mg.	7
301–400 gm.	126 mg.	9
401–500 gm.	210 mg.	7
Over 500 gm.	152 mg.	12

The failure of non-protein nitrogen to continue its progressive increase when the heart weight reaches maximum figures is an interesting observation whose significance will be discussed later in the paper in considering the relationship of non-protein nitrogen to blood pressure.

RELATION OF NON-PROTEIN NITROGEN TO HEART VALVES

Heart valves	Average N P N	No. of observations
Normal.	144 mg.	23
Slight lesions.	108 mg.	18
Marked lesions.	73 mg.	4
Extreme lesions.	49 mg.	4

Here the non-protein nitrogen varies inversely with the condition of the valves; that is, the more abnormal the valves the more normal the non-protein nitrogen. While this result would probably not hold for a larger series of cases, it certainly indicates that a poor circulation and chronic congestion of the kidney interfere little with the power of the kidney to excrete nitrogenous waste.

RELATION OF NON-PROTEIN NITROGEN TO MYOCARDIAL CHANGES

Myocardium	Average N P N	No. of observations
Normal.	106 mg.	40
Slight lesions.	233 mg.	3
Marked lesions.	204 mg.	3
Extreme lesions.	54 mg.	2

These results only indicate that myocarditis was an infrequent lesion in this series and that when it occurred it exerted no controlling influence on the non-protein nitrogen.

RELATION OF NON-PROTEIN NITROGEN TO CORONARY THICKENING

Coronaries	Average N P N	No. of observations
Normal	113 mg.	21
Slight thickening	116 mg.	15
Marked thickening	252 mg.	5
Extreme thickening	54 mg.	2

Here again there is no evidence of a significant relationship.

RELATION OF SYSTOLIC BLOOD PRESSURE TO CHANGES IN THE KIDNEYS

The blood pressure was taken in 38 of the 50 cases, so the conclusions are based on twelve less observations than in the cases of the non-protein nitrogen. When several readings were taken the highest only is used in my tables.

The outstanding relationship between blood pressure and kidney changes is its correspondence with the thickening of the renal arteries, a result made doubly striking by the fact that it does not correspond at all with the thickening of the coronary arteries. This concordance of blood pressure with renal arteritis is in accord with the work of Volhard and Fahr on renal sclerosis.

The tabulated results follow:

RELATION OF BLOOD PRESSURE TO KIDNEY WEIGHT

Kidney weight	Average blood pressure	No. of observations
Up to 270 gm.	179 mm.	12
270–300 gm.	142 mm.	6
Over 300 gm.	144 mm.	15

The somewhat higher average with small kidneys goes with the fact that arterial changes are apt to be maximum in atrophic organs. The same fact is brought out later in the table which shows that the arteries are thicker in kidneys of light weight.

RELATION OF BLOOD PRESSURE TO INFLAMMATORY EXUDATE IN THE KIDNEY

Exudate	Average blood pressure	No. of observations
None	123 mm.	7
Slight	151 mm.	13
Marked	144 mm.	11
Very large	197 mm.	7

RELATION OF BLOOD PRESSURE TO DEGENERATION OF THE RENAL EPITHELIUM

Epithelium	Average blood pressure	No. of observations
Normal	145 mm.	7
Slight degeneration	153 mm.	15
Marked degeneration	157 mm.	16

RELATION OF BLOOD PRESSURE TO GLOMERULAR CHANGES

Glomeruli	Average blood pressure	No. of observations
Normal	118 mm.	5
Slight lesions	132 mm.	8
Marked lesions	159 mm.	16
Extreme lesions	181 mm.	9

RELATION OF BLOOD PRESSURE TO INCREASE OF CONNECTIVE-TISSUE STROMA

Stroma	Average blood pressure	No. of observations
Normal	119 mm.	16
Slight increase	172 mm.	5
Marked increase	155 mm.	8
Excessive increase	200 mm.	9

RELATION OF BLOOD PRESSURE TO THICKENING OF RENAL ARTERIES

Arteries	Average blood pressure	No. of observations
Normal	121 mm.	14
Slight thickening	155 mm.	8
Marked thickening	180 mm.	12
Extreme thickening	206 mm.	3

This relative correspondence of various kidney lesions with blood pressure is more sharply brought out in a table

showing the average blood pressure in relation to normal structure and slight lesions grouped together and compared with the average blood pressure in marked and extreme lesions similarly grouped.

	Epithelium	Exudate	Glomeruli	Stroma	Arteries
Normal structure and slight lesions	150 mm.	143 mm.	126 mm.	132 mm.	133 mm.
Marked and extreme lesions	157 mm.	165 mm.	167 mm.	179 mm.	185 mm.

These figures show an interesting progression of correspondence between increasing kidney lesions on the one hand, and increasing blood pressure figures on the other. Epithelial changes stand at the bottom of this scale and arterial changes at the top. While it bears out Volhard and Fahr's conclusions about sclerosis of the renal arteries, it does not support their view that the glomerulus is to be regarded simply as a part of the vascular mechanism of the kidney.

RELATION OF BLOOD PRESSURE TO CHANGES IN THE HEART

The correspondence between increase in blood pressure and increase in heart weight is most evident. Hardly any other result could be credited because blood pressure is perhaps the most potent factor in cardiac enlargement in adult life. On the other hand, variations in blood pressure cannot be correlated with changes in the valves and myocardium.

It is surprising, however, that thickening of the coronary arteries does not go with high blood pressure in this series; the more surprising since thickening of the renal vessels and increasing blood pressure closely correspond.

RELATION OF AVERAGE BLOOD PRESSURE TO HEART WEIGHT

Heart weight	Average blood pressure	No. of observations
Up to 300 gm.	112 mm.	5
301–400 gm.	157 mm.	4
401–500 gm.	135 mm.	5
Over 500 gm.	189 mm.	12

RELATION OF AVERAGE HEART WEIGHT TO BLOOD PRESSURE

Blood pressure	Average heart weight	No. of observations
Up to 120 mm	350 gm.	8
121–150 mm	416 gm.	5
151–200 mm	571 gm.	7
Over 200 mm	590 gm.	6

These two tables show that the effect of blood pressure on heart weight is more definite than that of heart weight on blood pressure, and this result is to be expected, because high blood pressure almost always makes the heart big, but big hearts are caused by other things than high blood pressure.

RELATION OF AVERAGE BLOOD PRESSURE TO LESIONS OF THE HEART VALVES

Valves	Average blood pressure	No. of observations
Normal	162 mm.	21
Slight lesions	144 mm.	11
Marked lesions	120 mm.	1
Extreme lesions	146 mm.	4

The instances of severe lesions are few, but it is obvious that valve lesions do not necessarily increase blood pressure.

RELATION OF AVERAGE BLOOD PRESSURE TO MYOCARDIAL LESIONS

Myocardium	Average blood pressure	No. of observations
Normal	154 mm.	29
Slight myocarditis	155 mm.	3
Marked myocarditis	148 mm.	3
Extreme myocarditis	157 mm.	2

This table gives no evidence of any influence of myocarditis on blood pressure, and, were it not for the small number of cases showing myocardial lesions, would indicate that none exists.

RELATION OF BLOOD PRESSURE TO THE THICKENING OF THE CORONARY ARTERIES

Coronaries	Average blood pressure	No. of observations
Normal	143 mm.	16
Slightly thickened	172 mm.	10
Moderately thickened	151 mm.	5
Extremely thickened	157 mm.	2

This lesion does not go with an elevation of blood pressure in this series.

By leaving out of account the number of observations, the different effect of renal and coronary sclerosis on blood pressure can be compared as follows:

COMPARISON OF THE RELATION OF CORONARY SCLEROSIS AND OF RENAL SCLEROSIS TO BLOOD PRESSURE

Lesions	Average blood pressure with coronary artery lesions	Average blood pressure with renal artery lesions
Normal vessels	143 mm.	121 mm.
Slight sclerosis	172 mm.	155 mm.
Marked sclerosis	151 mm.	180 mm.
Extreme sclerosis	157 mm.	206 mm.

This result is very convincing and should induce further studies on the relation between local scleroses and blood pressure. There is a general idea that arteritis and blood pressure should go together, but there are many exceptions to this rule. It has not been my impression that thickened cerebral arteries have a very definite relation to blood pressure. The whole subject needs more understanding.

OTHER RELATIONS OF SYMPTOMS AND LESIONS

Eye Ground Changes. The eye grounds are apt to be looked at only when a change is expected, and so in this series their condition is recorded in only 19 cases, including 13 cases of nephritis and 2 of brain tumor.

Five of the nephritics showed definite neuroretinitis, while 5 other nephritics had entirely normal eye grounds. In comparing these two groups, both presented about the same degree of change in the kidney stroma and in the renal arteries.

The cases with normal grounds showed rather more albumin in the urine and a higher average non-protein nitrogen figure, 247 mg. as compared with 197 mg. The only striking difference between the two groups was in the blood pressure, an average of 245 mm. in the nephritic cases with neuroretinitis contrasted with an average of 161 mm. in those without. The series is entirely too small to form any judgment. The result is only given so that it can be included in larger series of other workers.

RELATION OF ALBUMIN IN THE URINE TO THE EXUDATE IN THE KIDNEY

This is obviously a comparison that rests on peculiarly uncertain data, for on the one hand, it is the junior or substitute interne who examines the urine, while on the other hand, to judge how much exudate exists throughout both kidneys by how much is seen in one section cannot give reliable results. In this series there is shown, however, a rough correspondence between the exudate in the urine during life and the kidney after death. No case with no albumin in the urine showed an excessive exudate in the tubes, and every case with a urine that boiled solid showed some exudate in the kidney. In general the cases with smaller amounts of albumin in the urine showed less exudate in the kidney than those with larger amounts of albumin. More than this cannot be said.

There is, however, in addition, an apparent connection between the amount of albumin in the urine and the average kidney weight; thus, in 19 cases, with no albumin or a trace only, the average weight of the kidney was 313 gm., while in 15 cases showing a precipitate or boiling solid, the average weight was 371 gm. It is not improper to infer that an exudate within the kidney in part explains this difference, especially as there is no significant relation of albumin in the urine to other kidney changes, i. e., to epithelial, glomerular, stromal or arterial lesions. It is worth noting that Volhard and Fahr's contention, that epithelial degeneration is the basic cause of albumin in the urine, is not borne out, for in this series of cases there was a complete absence of relationship between these two phenomena.

Dropsy in this series shows little tendency to vary in degree with the amount of kidney lesion or with the changes in any one element of the kidney more than another, except that epithelial changes seem to have less relation to it than other kidney lesions.

Dyspnea, on the other hand, tends more definitely to increase with increasing kidney lesions, least with epithelial and most with arterial changes.

The relation of symptoms to each other does not require autopsies for its study and a small series such as the present is fruitless for general purposes. It may be stated, however, that the non-protein nitrogen and blood pressure show some but not a striking, tendency to vary together. The smaller increases of non-protein nitrogen over normal in this series go with a progressive increase of blood pressure, but as the non-protein nitrogen rises to higher levels the blood pressure fails to maintain a corresponding increment. Thus:

RELATION OF AVERAGE BLOOD PRESSURE TO NON-PROTEIN NITROGEN

N P N	Average blood pressure	No. of observations
Up to 30 mg.	127 mm.	4
31–50 mg.	136 mm.	14
51–100 mg.	173 mm.	6
101–200 mg.	165 mm.	6
Over 200 mg.	171 mm.	8

There seems to be an explanation of this failure of blood pressure to follow the higher non-protein nitrogen figures in the two kinds of nitrogen retention. The first kind of uremia is due to a gradual failure of the power of the kidney to get rid of the nitrogen which enters the blood in twenty-four hours. This demands a stronger physiological stimulus in order to maintain a nitrogen balance and this stimulus is supplied by a greater concentration of non-protein nitrogen in the blood. This accounts for the elevated non-protein nitrogen figures which often remain comparatively constant for weeks or months. This process seems to go hand in hand with the loss of glomeruli and tubules, and the corresponding increase of stroma in the kidney. This lesion is regularly

accompanied by a thickening of the renal arteries with which an increase of the blood pressure goes along as has been indicated above. So it happens that up to a certain point we should expect this corresponding increase of non-protein nitrogen and blood pressure which has been noted by every observer of kidney disease.

There is, however, a second type of uremia and one which usually becomes controlling in the very high non-protein nitrogen cases. This second type depends on the inability of the kidney to concentrate the solution of urea and other nitrogenous waste products in the urine. This power weakens rather rapidly under strain, so that ordinary volumes of urine are insufficient to carry off the twenty-four hour waste, and the residue is retained in the body and, in part, piles up in the blood. The process advances rapidly and yields high non-protein nitrogen figures within a week or ten days and causes a uremic death from true retention. It occurs in damaged kidneys after sudden strains such as surgical operations and the like, and is often a final and fatal complication in a chronic nephritis. It causes the high and fatal non-protein nitrogen figures, but not, so far as I know, an increased blood pressure. Thus it happens that moderate and persistent elevations of non-protein nitrogen are apt to be associated with progressive increases of blood pressure, while rapid, very high and terminal elevations of non-protein nitrogen are not associated with corresponding elevations of blood pressure. This is so in this series and I believe it will prove substantially true for larger series also.

The relation of lesions to each other also needs only a large series of autopsies independent of clinical data for its study. Certain observations may be worth recording, however.

The kidney weight varied inversely with the amount of new connective tissue and with the thickening of the renal vessels. In other words, as the stroma increases and the vessels thicken there is probably a loss of the secretory elements of the kidney which overbalances the gain in stroma and which is not compensated for by an increase in exudate. This presumably goes along with a loss in volume, although this was not studied in this series.

RELATION OF AVERAGE KIDNEY WEIGHT TO INCREASE OF STROMA

Stroma	Average kidney weight	No. of observations
Normal	327 gm.	14
Slight increase	307 gm.	9
Marked increase	343 gm.	8
Great increase	285 gm.	12

RELATION OF AVERAGE KIDNEY WEIGHT TO THICKENING OF RENAL ARTERIES

Renal arteries	Average kidney weight	No. of observations
Normal	377 gm.	17
Slight thickening	354 gm.	10
Marked thickening	256 gm.	12
Extreme thickening	240 gm.	3

Epithelial changes, on the other hand, which almost always result in a swelling of the cells, do not in this series induce a definite and progressive gain in the kidney weight.

RELATION OF AVERAGE KIDNEY WEIGHT TO DEGENERATION OF THE EPITHELIUM

Epithelium	Average kidney weight	No. of observations
Normal	348 gm.	6
Slight changes	280 gm.	17
Marked changes	364 gm.	20

Increasing amounts of exudate, as estimated from the study of the sections, while showing some correspondence with increasing kidney weights, do not yield a convincing relationship.

RELATION OF AVERAGE KIDNEY WEIGHT TO EXUDATE IN THE KIDNEY

Exudate	Average kidney weight	No. of observations
None	304 gm.	9
Slight	312 gm.	11
Marked	362 gm.	15
Extreme	318 gm.	8

The heart weight, which reveals chiefly the mass of cardiac muscle, did not vary as much with the disease of the valves

or with coronary thickening as with changes in the kidney, especially with thickening of the renal vessels. This last relation was to be anticipated because of the above discussed relations of blood pressure to renal vessels and to heart weight respectively.

RELATION OF AVERAGE HEART WEIGHT TO VALVE CHANGES

Heart valves	Average Heart weight	No. of observations
Normal	477 gm.	18
Slight valvulitis	402 gm.	10
Marked valvulitis	341 gm.	4
Extreme valvulitis	573 gm.	3

RELATION OF AVERAGE HEART WEIGHT TO CORONARY THICKENING

Coronary arteries	Average heart weight	No. of observations
Normal	379 gm.	17
Slight thickening	509 gm.	10
Marked thickening	528 gm.	4
Extreme thickening	390 gm.	1

RELATION OF AVERAGE HEART WEIGHT TO THICKENING OF RENAL ARTERIES

Renal vessels	Average heart weight	No. of observations
Normal	355 gm.	15
Slight thickening	434 gm.	6
Marked thickening	539 gm.	12
Extreme thickening	645 gm.	2

The relation of heart weight to kidney weight shows only a moderate tendency for the heart to increase in size as the kidney weight departs from normal either up or down.

RELATION OF AVERAGE HEART WEIGHT TO KIDNEY WEIGHT

Kidney weight	Average heart weight	No. of observations
Normal: 270–300 gm.	409 gm.	7
Less than normal	457 gm.	13
Greater than normal	437 gm.	14

SUMMARY

The data in this paper indicate (1) that an increase in non-protein nitrogen is more closely associated with an increase in the kidney stroma than with any other of the renal lesions here studied, and (2) that an increase of blood pressure and of heart mass are more closely associated with thickening of the renal arteries than with any other lesion here studied, whether in the heart or kidney.

The results are founded on data too few in number and too poorly controlled to justify anything approaching a final judgment. The work is put forward as a contribution to present kidney problems.

ORGANIZATION OF PNEUMONIC EXUDATES*

ROLFE FLOYD, M.D.

THE purpose of this paper is (*a*) to show how the exudate in the lung alveoli starts to change into connective tissue, and (*b*) to throw light on the relation of organizing pneumonia to acute lobar pneumonia.

The organization into vascular fibrous tissue of intra-alveolar lung exudates, especially as this occurs in wide areas following an acute lobar pneumonia, has been extensively studied. Important contributions have been made by Laënnec,[1] Marchand,[17] Cohn,[31] von Kahlden,[32] Herbig,[33] Ribbert,[41] Cornil,[42] Vogel,[43] Delafield,[56] Milne,[74] Kidd,[75] Kline[79] and others.

It has been determined that the intra-alveolar exudate of fibrin, including the exuded cells in its meshes, shrinks and condenses, thus leaving a space between it and the alveolar wall, though retaining contact with the wall by adhesions which may be either extensive or slender and filamentous. These connections between the retracted fibrin plugs and the wall may be formed of fibrin or of elongated cells. The fibrin, when originally deposited, is often continuous from space to space through the pores of Cohn,[31] which establish fine connections between adjacent air spaces belonging to different infundibula, and, when general retraction of the fibrin exudate occurs, these communicating strands stand out very distinctly. Pulmonary epithelium and other exuded cells appear in the gaps between the plugs and space walls, and some of the flattened epithelial cells, which have a spindle form when seen on edge, are often applied to the plug surface. About two weeks after the onset of the pneumonia, cells with elongated nuclei, exhibiting all transitions to fibroblasts, appear within the substance of the fibrin plugs and on their surface. At this time, or a little later,

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capillary vessels given off from the capillaries of the space walls enter the plugs by traversing the above-described adhesions between the space wall and plug. This process and also the communicating bands which traverse Cohn's pores, and later are changed into connective tissue, have been demonstrated beyond doubt by means of serial sections by MacCallum[60] and others. As time passes the fibrin is more or less completely absorbed and replaced by fibrillated connective tissue, and then the appearance of two networks is produced in sections, one the alveolar walls and the other the organized intercommunicating exudate. The alveolar walls also show varying degrees of fibrous thickening which may reach the point of obliterating the gaps between them and the fibrin plugs, so that the distinction between organized exudate and basic lung structure, that is, between the two networks, is completely lost and the whole tissue changed into a dense connective-tissue mass, devoid of spaces, tough and airless.

There has been much discussion about the origin of the connective tissue in the plugs, some observers thinking it an ingrowth either from the pleura and interlobular septa (Eppinger,[11] Cohn[31]), or from the bronchiole walls (Ribbert,[41] Herbig[33]), or from the walls of the air spaces (von Kahlden[32]). Others have thought that fibrogenic cells migrated into the plugs (Aufrecht,[40] Cornil[42]), or that a late secondary exudation of fibroblasts occurred not evoked by the original bacterial irritant (Ziegler,[65] Josephson[24]), or that cells originally exuded changed into fibroblasts (Marchand[17]). Still others have believed that the pulmonary epithelium surrounded and entered the plugs and became connective-tissue cells (Woronochin,[8] Lindermann[26]), but this view has never been generally accepted. Perhaps the strongest current of recent opinion sets toward the derivation of the connective tissue, along with the vessels, from the wall of the air space in which each plug lies, though extensions of connective tissue into the plugs from pleura, interlobular septa and bronchiole walls, confirmed by various observers, are regarded as established but exceptional phenomena.

Organization of intra-alveolar exudates, as described, has been observed in bronchopneumonia, in tuberculous con-

solidation and about infarcts and abscesses (Frankel[36]), but its most extensive development, and that which has attracted the most attention, is as a sequel of lobar pneumonia. Here the lesion is seldom coextensive with the original pneumonic exudate, but involves portions only of the lung originally inflamed.

The question whether the lobar pneumonias which go on to organization are a separate type of lesion from the outset or whether appropriate causes may effect this change in any lobar pneumonia is still undecided. Those who hold the latter view name as causes debility (Heschl,[5] Milne[74]), alcoholism (Marchand[17]), presence of excess of fibrin (von Kahlden[32]), excessive sluggishness of the lymph circulation (Köster[19]), insufficient pus cells in the exudate to effect its absorption (Flexner[54]) and the presence of an excess of serum (Kline[79]).

My contribution is based on the study of two sets of material, namely, (*a*) 603 lung sections, practically all showing pathologic changes of some kind, obtained from 249 cases whose autopsies I either did or attended. In many of these cases I studied the patients during life, and in all of them there are full clinical, autopsy and microscopic records; (*b*) 153 lung sections given me by Dr. Delafield, obtained by him at autopsy, all showing some lesion. In only a few of these, however, are clinical and pathologic records available.

Before analyzing the observations on this material it is necessary to define what an intra-alveolar connective-tissue plug is and to discuss briefly some general characters of pneumonic exudates.

A typical connective-tissue plug of fairly recent origin, perhaps two or three weeks old, is composed of a dense, refractive substance taking a strong eosin stain. It is of a finely granular structure and may also show a distinct fibrin reticulum, either compact or, in places, more open (Fig. 22). The plug does not fill the alveolus in which it lies but regularly leaves a residual space which may be empty, or may contain polynuclear, mononuclear, blood or epithelial cells. Some flattened epithelial cells are often applied to the plug surface and have a spindle form when seen on edge. In sections a plug may appear to lie free in the alveolus, or

it may be connected in part to the alveolar wall, either through broad areas of contact or by slender strands or bridges of fibrin or of cells. Tenuous strands may also extend through mural pores and so connect the plug to plugs in neighboring spaces (Fig. 23). The dense plug substance often looks incompletely separated into rounded

FIG. 22. Organizing pneumonia, death on the twentieth day. Typical organizing fibrin plug adherent to the alveolar wall at A, but leaving a residual space elsewhere. Elongated fibroblast nuclei may be seen in the plug. × 263.

masses by partial fissures. In the plug are regularly included nuclei, some polynuclear and often pyknotic and deformed; others large, vesicular and rounded; and finally oval or distinctly elongated vesicular nuclei which can be seen in all stages of elongation until they appear as fibroblast

nuclei with their cell bodies and associated fibrils sharply distinct (Fig. 22). When simply oblong without defined cell body these early fibroblasts do not resemble the epithelial cells applied to the plug surface, but when the long cell bodies appear, and before the characteristic fibrillar ground substance is deposited, I know of no way of distinguishing

Fig. 23. Organizing pneumonia. Slender fibrin strand connecting adjacent plugs through a Cohn pore. × 213.

the early fibroblasts which lie near and parallel to the surface, from the epithelial cells lying against the plug, as above described (Fig. 24). It is evident that in this difficulty lies the origin of the belief of some observers, above referred to, that epithelium may be metamorphosed into connective tissue. Fibroblasts deep in the plug substance, however, and

penetrating it in different directions, may, I believe, be safely identified as such.

I have gained the impression that pyknotic and deformed nuclei are more numerous in early plugs, twelve days or so old, than in late ones, three or four weeks old, and that some of the cells in the plugs, especially the polynuclears, are

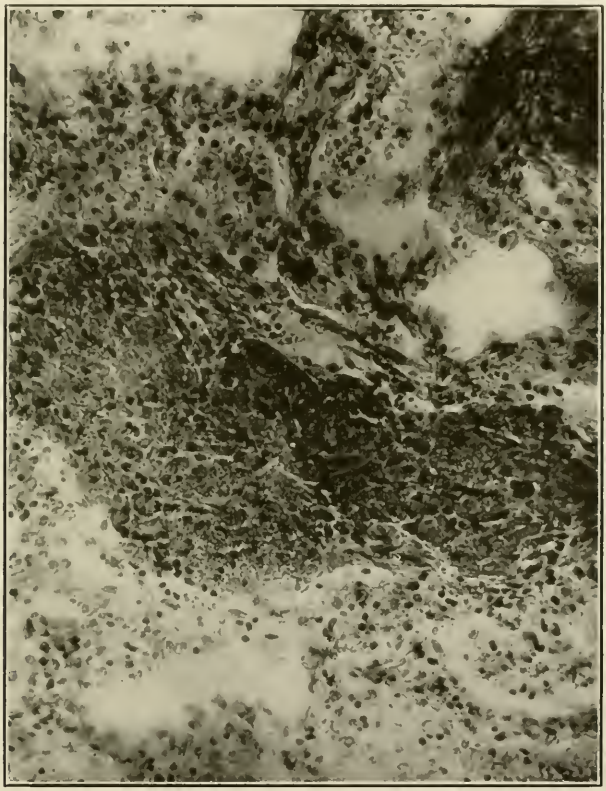

Fig. 24. Organizing pneumonia, death on the twentieth day. Spindle-shaped cells along the plug edges, some separate and some adherent; impossible to say which are epithelium and which fibroblasts. × 213.

destroyed and disappear, while some of the mononuclears go on to develop into fibroblasts (Fig. 25).

Blood-vessels budding from mural capillaries unquestionably penetrate these plugs, but I am convinced that they do

not penetrate them all or even a majority of them in the early stages, that is, not until after four or five weeks.

When occurring in any number, the dark red anastomosing plugs with elongated nuclei and fibroblasts are strikingly evident at the first low-power glance (Fig. 26), but in order to determine whether there is definite evidence that the

Fig. 25. Pneumonia secondary to bronchoesophageal fistula. Fibrin plug with some elongated nuclei and many pyknotic polynuclear nuclei. × 213.

exudate in a particular alveolus promises to organize and so shall be considered an early connective-tissue plug, certain criteria must be set up. It is evident that the amount of retraction and of condensation of the fibrin is not a significant feature and will be the less developed the earlier the

stage of the process. It is also evident that the same will be true of the ingrowing capillaries.

Every alveolus which contains reticulated fibrin or a dense granular mass of exudate with a strong affinity for eosin and elongated vesicular nuclei in the fibrin mass, exclusive of those which may be confused with epithelium

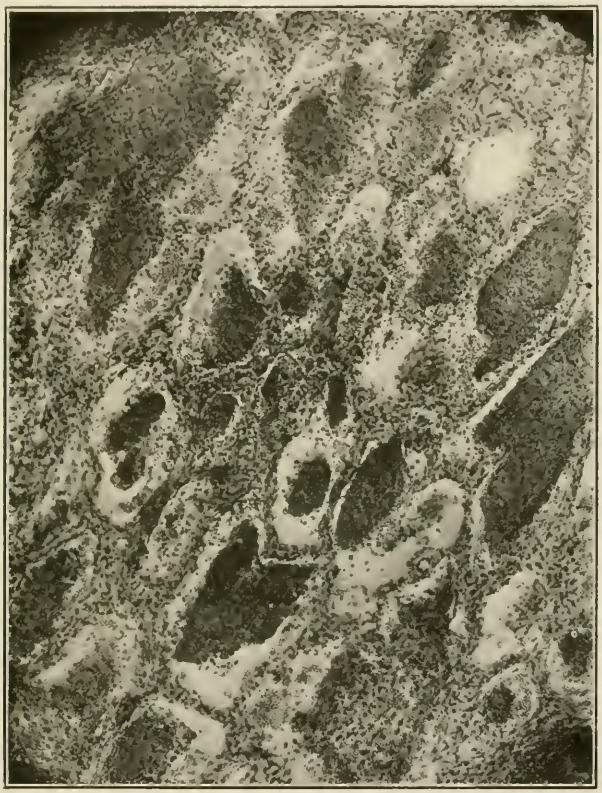

FIG. 26. Organizing pneumonia, death on the twentieth day. Typical organizing intra-alveolar plugs with some thickening of the alveolar walls. × 63.

as above described, promises organization of its exudate, and has been considered to contain an early connective-tissue plug in the present study.

In order to justify this statement it is necessary to consider certain components of pneumonic exudates.

Fibrin varies greatly in quantity. Only rarely does it occupy as much or more space than the cellular elements as a whole. It may be totally absent, so far as this can be established, through the absence of any demonstrable strands, fibrillae or reticulum in the spaces. It not infrequently is very unevenly distributed, occurring in large and even overwhelming quantity in a few spaces and scarcely recognizable

Fig. 27. Lobar pneumonia, death on the eighth day. Fibrin concentrated in alveoli along a large vessel and mostly on the side of the spaces next the vessel sheath. × 40.

in most of the rest. Moreover, it is frequently asymmetrically deposited in individual spaces, forming a dense reticulum on one side and fraying out to fine isolated fibrils in the opposite portion (Fig. 25). Such asymmetrical concentrations apparently often form the basis of connective-tissue plugs. In many sections I have observed such concentrations along the pleural boundaries, the fibrin being regularly denser on the side next the supporting tissue (Fig. 27). The same observation

has been made by Cornil.[12] I can suggest no reason unless these portions of the alveoli move less with respiration, and so the fibrin is less stretched and less insufflated by the tidal air during its deposition. The subsequent formation of plugs in such regions, to the exclusion of others, perhaps explains the view advanced by some observers that the connective

FIG. 28. Lobar pneumonia. Fibrin plug without fibroblast nuclei. × 213.

tissue of the plugs is derived from pleural and trabecular connective tissue. At any rate the fibrin is usually unequally distributed, a lot in some spaces, very little in others and often asymmetrically deposited in individual spaces, so that a partial absorption of the exudate would result in leaving fibrin plugs only partly filling the spaces, a probable factor

in plug-production as well as subsequent shrinkage and condensation. It is not at all unusual to see sections, especially of pneumonias dying within two weeks of their onset, with a large number of typical dense red staining fibrin plugs which show no elongated nuclei (Fig. 28). Whether these represent the earliest stage of connective-tissue plug formation, and whether fibroblasts would subsequently have appeared in them had life been prolonged, as Delafield[56] thought, I have no way of knowing. At any rate they are excluded by the above definition from the plugs with indications of organization. There is no obvious reason why they cannot be absorbed as well as any other fibrin exudate.

Serum is coagulated in various forms by hardening agents and appears in lung sections as fine granular matter, as a foam work or as a homogeneous coagulum enclosing cells and some round lacunae, presumably air bubbles. When in the latter form it may stain very faintly or very strongly with eosin, apparently depending on how much blood pigment it held in solution when coagulated. Kline,[79] as a result of experiments on dogs, inclines to the belief that serum is an essential factor in the production of organizing pneumonia; but I have never seen lon vesicular nuclei or fibroblasts in even the deepest staining serum coagula in lobar pneumonia, and almost never in sections of other lesions. One most striking alveolus from an organizing pneumonia contained a homogeneous serum coagulum, in the central part of which was included a distinct wisp of fibrin fibrillae. In the serum were several cells with round vesicular nuclei but none elongated, while those in the fibrin were definitely elongated and of the early fibroblast type (Fig. 29). I can see no reason for believing that exuded serum favors the development of fibroblasts as exuded fibrin does.

The relations of the exuded cells to the connective-tissue plugs are various. Red blood cells are often included in the plugs, but in no section did fibroblasts appear in alveoli filled with blood alone even when it had probably been there for some time.

Polynuclears are, of course, entangled in the reticular fibrin or included in the dense plugs, often in large numbers;

but they seem to exert no influence on organization. In fact, as above mentioned, they undergo degeneration with pyknosis of their nuclei (Fig. 25), mostly before the end of the second week from the onset in lobar pneumonia, so that after that time few are seen in the plugs.

FIG. 29. Organizing pneumonia, death on the thirteenth day. Large alveolus filled with coagulated serum, with a mass of fibrin in the center. The nuclei in the serum are round; some of those in the fibrin are distinctly elongated. × 213.

The epithelium is often seen applied to the plug surface, as above mentioned (Fig. 24), whether as a result of simple desquamation from the space wall or by a true investing proliferation, as has been thought by some observers, it is difficult to be sure. The difficulty of distinguishing such cells

from fibroblasts has already been explained. Sometimes definite dense retracted plugs with typical long vesicular nuclei occur where no reticulated fibrin can be demonstrated in any of the alveoli in the section, but where there is much desquamated epithelium, and all stages can be traced from loose, discrete, desquamated epithelial cells in some alveoli

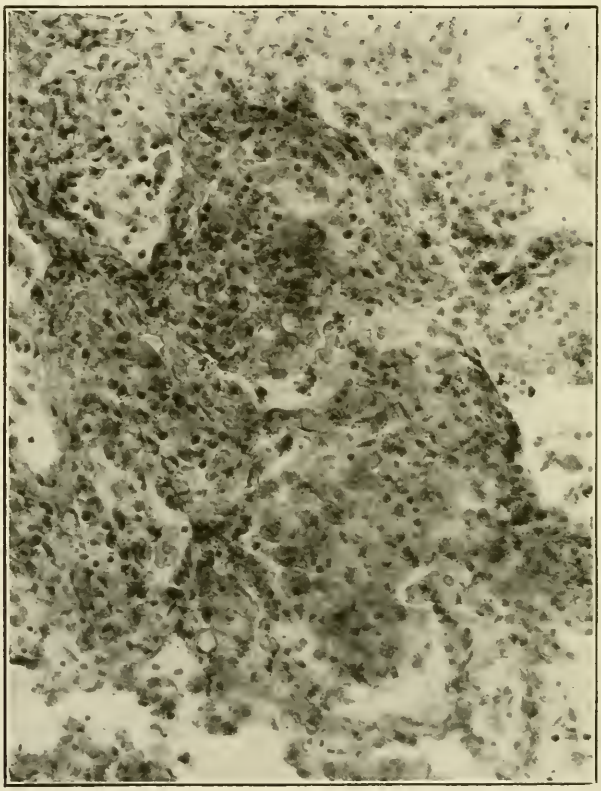

Fig. 30. Secondary bronchopneumonia in an adult. Much epithelium in the alveoli, in one case concentrating to form a plug. Fully formed plugs with elongated nuclei and traces of their epithelial composition still distinguishable occur in the same section. × 213.

to their conglomeration into dense plugs in others, in some of which elongated nuclei occur (Fig. 30). Thus the formation of organizing plugs out of epithelium instead of fibrin apparently occurs, though rarely. Of course, some fibrin-binding

substance may be present in such cases without presenting the usual reticulated appearance.

As already stated the fibroblasts are derived from cells with a single rather large vesicular nucleus. Much has been written about such cells in inflammatory processes, and I have no new light to throw on their origin. They presumably belong to the mesenchyme group, and I believe they exist in the intra-alveolar exudate from the start rather than that they represent a secondary migration induced by a new stimulus, because they lie deep in the dense fibrin plugs when they first take on the oblong shape. Mononuclear cells occur in most intra-alveolar exudates—some have no visible cell body and a small dense nucleus, the lymphocyte or round-cell type; some have a larger vesicular nucleus and an appreciable cell body, the endothelial type, and may be hard to distinguish from pulmonary epithelium. How many kinds of cells the mononuclears represent, from how many sources of origin, whether they arrive through the blood or lymph channels, what their various functions and destinies may be, is still somewhat uncertain. That one group of them may become fibroblasts, however, is generally accepted. The only new ideas I have to offer about them in organizing pneumonias is that they exist in the exudate from the start (a suggestion made long ago by Marchand[17]), that the presence of fibrin in some way favors their change into fibroblasts and that this change is not dependent on the ingrowth of buds from mural capillaries because fibroblasts regularly begin to develop before any vessels appear and may often attain full development where no vessels can be demonstrated. If the fibroblasts were derived from the mural connective tissue by ingrowth, as the vessels are from the mural capillaries, it should be easy in early stages to see spots in the plugs from which the connective tissue radiated, an appearance I have not seen, instead of a simultaneous change in shape of nuclei scattered all through the plug, which is the usual appearance.

Just as fibrin plugs may be present in many spaces without the presence of any elongated vesicular nuclei, so cells with such nuclei and even definite fibroblasts may occur in the alveoli, without any fibrin and without any plug formation;

but I have not met this condition in lobar pneumonia or secondary patchy pneumonia, though in tuberculous lungs it is not very rare (Fig. 31).

The new blood-vessels, about which so much has been written and the manner of whose ingrowth has been demonstrated beyond question in serial sections by MacCallum[50]

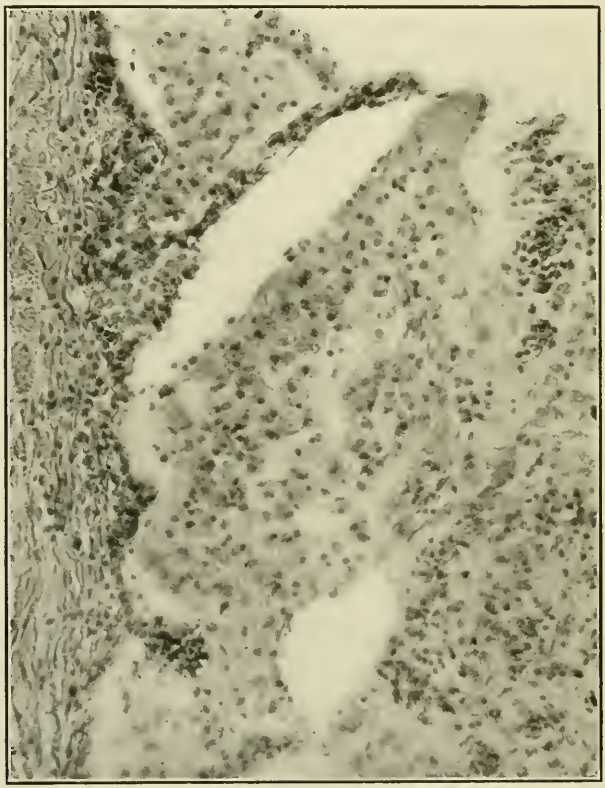

Fig. 31. Subacute phthisis. Fibroblasts growing in an alveolus with no fibrin and no condensation of the cellular exudate into a plug. × 213.

and others, have not proved as universal as I expected. In fact, not only have they been absent from entire sections showing early plugs with definite early fibroblasts, but quite difficult to find in some lesions of long standing, notably in a case of four and a half months' duration.

Conservatism must be exercised in interpreting vessels as newly formed and pathologic, for the vessels in the normal partitions which partially separate the alveoli springing from the same infundibulum often appear to penetrate or jut into the plugs just as they do in any exudate that occupies the alveoli (Fig. 26). On the other hand, small thin-walled

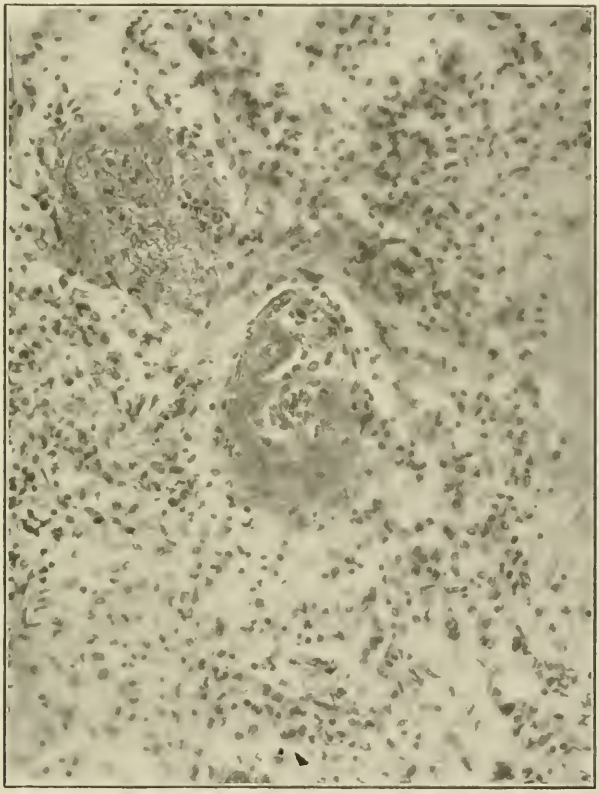

Fig. 32. Pneumonia secondary to bronchoesophageal fistula. New-formed vessels in an organizing fibrin plug. × 213.

single vessels cut in cross section, or short and isolated oblique slices lying in the central portion of the plugs, are definitely newly formed and inflammatory (Fig. 32). This opinion that new-formed vessels in the plugs are not essential and, in many cases, not even a frequent feature of the lesion

under discussion, is based not only on the study of ordinary hematoxylin-eosin preparations but also from the careful examination of a number of sections of organizing pneumonias among the slides received from Dr. Delafield, in which he injected the pulmonary vessels with a gelatin Prussian-blue mass, in which the capillary ramifications may be accurately traced.

Connective-tissue plugs, as above defined, are by no means rare in the material studied. They appear in 129 out of my 603 sections and in 48 out of the 153 made by Dr. Delafield, that is, in 23.4 per cent, or over ¼ of all sections examined.

The term organizing pneumonia has been applied to cases in which the organizing intra-alveolar plugs are numerous, the lesion of lobar distribution and not tuberculous in origin, especially of the patient first falls sick as a lobar pneumonia. Nine of my cases fall in this group, and it is from them that the sections diagnosed as organizing pneumonia were taken. A study of the records of these cases does not support the view of some observers that old age and debility are important etiologic factors. Thus the average age is forty years, the youngest twenty, the oldest seventy-two, and only 1, the last mentioned, over sixty. The nutrition and previous general health, as far as it can be determined from the records, was fair or good in all but 2. Excessive use of alcohol is reported in only 1 case. Seven out of 9 of my series were males. The onset was sudden and identical with that of ordinary lobar pneumonia in 6, but of a more gradual character in 3, the most indefinite being in the old man of seventy-four years, who was, however, feeble-minded and unable to give a reliable account of himself, and of the other 2, one in a man, very sick, who was taken ill three months before admission, where recollection of the type of onset could well have been confused.

There is nothing significant about the location of the consolidation, as is evident from the following table:

Entire right lung, 3.
Entire left lung, 2.
Entire left and part of right lung, 1.
Right upper and middle lobes, 1.

Both lower lobe, 1.
Right upper lobe, 1.
Left lower lobe, 1.

In 6 cases there were fibrous pleural adhesions; in 2 cases a fibrin exudate. The duration varied from eight to one hundred and thirty-five days, the average from 8 cases being forty days. Other lesions of lung and pleura were frequently present, abscesses or cavities or both occurring in 5 cases and a double empyema in a 6th one. The microörganism was determined in only 2 cases: 1 a pneumococcus Type I and the other a pneumococcus Type II.

The intra-alveolar plugs themselves present different stages in the process already described in detail. As has been above indicated new vessels in them are not frequent, being notably hard to find in the case of a hundred and thirty-five days' duration, and found in only 3 others of the series, 1 of uncertain duration and the other 2 of thirteen and thirty-five days respectively.

This series of 9 organizing pneumonias is very similar in general to other series that have been reported, though the case of eight days' duration is a very early one. Cavities, abscesses and pleural adhesions have been many times observed as concomitant lesions. I have given this recapitulation of my cases not to illustrate any new features, but rather to show that my observations are based on true cases of organizing pneumonia similar to those reported by other observers.

It is evident not only from my small series but from the literature that organizing lobar pneumonia is not a rare lesion at autopsy. On the other hand a healed lesion corresponding to it, that is, a lobe extensively changed into connective tissue, is a decided rarity. Such cases when found may be impossible to distinguish from cases which have started as bronchopneumonias or from cases primarily pleurogenic. I have seen but one such case in an adult with extensive fibrosis of the lung tissue and multiple large bronchiectasiae involving the right upper and middle and the left lower lobes in a woman, aged forty-eight years, without any history of previous lung trouble.

The deduction from all this is that organizing lobar pneumonia, once fully established, proves fatal in the vast majority of cases.

Organization of the intra-alveolar exudate, however, is not at all confined to sections from cases in which the lesion is pronounced enough to be called organizing pneumonia, as shown by the following list of the anatomic diagnoses of the sections in my own series which show organizing plugs:

Organizing pneumonia	31
Lobar pneumonia	38
Bronchopneumonia	5
Secondary or patchy pneumonia	5
Tuberculosis pneumonia (all forms)	27
Interstitial pneumonia	6
Infarcts	5
Lymphatic leucemia	3
Congestion and edema	3
Pneumonia secondary to bronchoesophageal fistula	1
Chronic congestion with heart disease	1
Cancer	2
Compressed lung beneath empyema	1

The incidence of organizing plugs in the ordinary forms of consolidation is shown in the following table, again from my own series:

	Total number of sections exhibiting this lesion	Number of sections of this lesion which show organizing plugs	Sections of this lesion showing organizing plugs, per cent
Lobar pneumonia	101	38	37.6
Bronchopneumonia	55	5	9.9
Secondary or patchy pneumonia	59	5	8.4
Tuberculous pneumonia (all forms)	87	27	31.3

Organizing plugs are most frequent in lobar pneumonia, and here also the fibrin plugs without early fibroblasts are most often seen. Of 16 sections in which fibrin plugs without fibroblasts occur, 9 are in sections of lobar pneumonia. In lobar pneumonia dense fibrin, one of the components of organizing plugs, is present in some alveoli in nearly half the sections, and in many such specimens some elongated

cells appear in the fibrin. There is thus more or less incipient organization of the exudate in over one-third of all lobar specimens examined, but the lesion does not reach sufficient development or extent to warrant calling it organizing pneumonia. In other words, the sections of lobar pneumonia and of organizing pneumonia, taken together, apparently represent a series exhibiting various degrees of organization from none up to the extensive examples, and the line of definition between lobar pneumonia and organizing pneumonia becomes an arbitrary one. Numerically stated, of 134 sections of lobar consolidation 54 show no tendency to organization, though fibrin and mononuclear cells regularly occur in the exudate; 9 show distinct dense fibrin plugs but no elongated nuclei; 38 show organizing plugs but not in sufficient numbers to be called organizing pneumonia; while 33 must be considered frank organizing pneumonia.

The proportionate figures hold also in general for the cases from which these sections were taken: of 48 cases of lobar pneumonia, 24 showing no organization, 15 showing minor amounts of organization and 9 being classed as organizing pneumonia.

On this basis I believe that organizing pneumonia, or the "lobar pneumonia with connective tissue" of Delafield, is not a separate lesion or disease but rather a variety of lobar pneumonia, the extreme expression of tendency that exists in many cases of lobar pneumonia.

In bronchopneumonia organization of the exudate in the bronchial wall is, of course, very frequent, but the formation of the connective-tissue plugs here under discussion is comparatively uncommon—5 times in 55 sections in my series. Age may be a factor, though typical plugs are present in sections from an infant under one year. In the Delafield sections there are several from persistent bronchopneumonias in adults in which organizing fibrin plugs form a prominent feature of the lesion (Fig. 33).

In the secondary patchy consolidations which occur as terminal lesions in many conditions, especially in adults, intra-alveolar organization is again comparatively uncommon, 5 sections out of 59 in my series. In these cases there is in general more serum and red cells and less fibrin, but how

much this composition of the exudate has to do with a relatively smaller number of plugs, I do not know.

In tuberculous inflammations of the lung, on the other hand, a large proportion of the specimens, 27 out of 87, show organizing fibrin plugs, and in some cases of phthisis the lesion seems to be based on the development of connec-

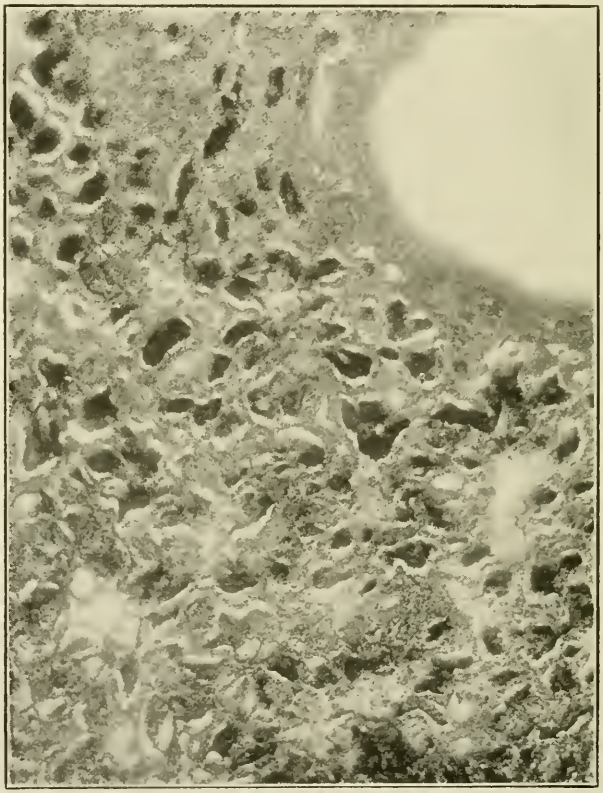

Fig. 33. Persistent bronchopneumonia in an adult. Many organizing plugs in alveoli near an inflamed bronchus. × 35.

tive-tissue plugs in nearly every alveolus, necrosis of this exudate subsequently occurring over areas of varying extent (Fig. 34). Here mononuclear cells are often predominant in the exudate, and instances in which they are changing into fibroblasts in spaces in which no fibrin and no plug

substance are present are not very unusual. In lobar pneumonia the dense fibrin plugs are common and the fibroblasts comparatively rare; in tuberculous pneumonia, on the contrary, I have found the fibroblasts numerous, even developing when there is no fibrin, and when fibrin is exuded, fibroblast nuclei readily develop in it.

FIG. 34. Tuberculous pneumonia. Organizing plugs in many spaces. × 35.

Organization of the pneumonic exudate has generally been regarded as beginning about the fourteenth day after the onset of the symptoms, perhaps because it was thought that the new connective tissue was derived from the alveolar wall along with the budding capillaries which are first demonstrable at about this date. Cornil,[42] however, describes

elongated fibrogenic nuclei on the seventh day in human pneumonia, and on the sixth day in experimental pneumonia in dogs. My belief that the fibroblasts develop from cells contained in the original exudate, especially in the presence of fibrin, but antecedent to and quite independent of the vascularization of the plugs, is confirmed by finding elon-

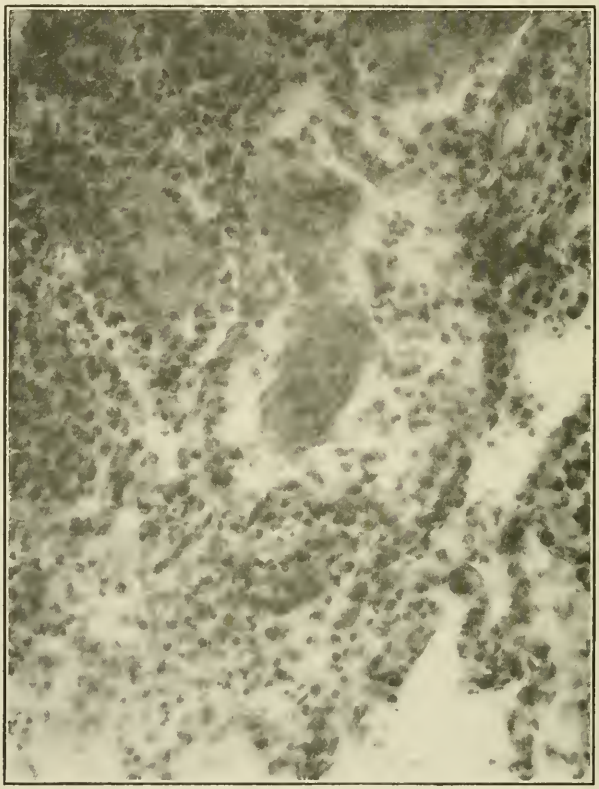

Fig. 35. Lobar pneumonia, death on the fifth day. Fibrin plug with elongated nuclei. × 263.

gated vesicular nuclei in fibrin plugs in 2 cases of lobar pneumonia dying on the fifth day (Fig. 35) and in 2 other cases dying on the sixth day, and also 1 case, classed as organizing pneumonia, dying on the eighth day.

There is an obvious objection to the ideas here presented, namely, the fact that, clinically, cases of organizing pneu-

monia are decidedly unusual, while complete resolution occurs in the vast majority of the lobar pneumonias that recover. Moreover, in those of my cases which died, where the duration of the disease was known, the average day of death in those with no organization or with plugs in which the nuclei are not typically elongated, was the eighth day, while in those with organizing plugs it was the ninth day — not a significant difference. There is no evidence, however, and no reason to suppose that the presence of oblong or oval nuclei in a plug of intra-alveolar fibrin interferes in any way with its complete solution, or that the condition which exists in a lobar pneumonia when it contains many such plugs is any more resistant to resolution up to about the fourteenth day than the cases with no indications of organization. After the cells have fairly become fibroblasts, on the other hand, and especially after the deposition of fibrillar ground substance, usually somewhere between the fourteenth day and the twenty-first day, resolution must become progressively more difficult in that part of the consolidation where such organization is proceeding.

Another objection to the theory here presented is that organization of a few intra-alveolar plugs would seem not unlikely in many cases of lobar pneumonia, for there are numerous cases in which some signs and some roentgen-ray shadows persist after three weeks, to clear up gradually but completely later on, and in such lungs there ought to be left some traces of the process. It is, however, well established, on the other hand, that resolution may be delayed and sluggish without any organization of the exudate or without its development to the true fibroblast stage, and, on the other hand, a few scattered alveoli changed into connective tissue would be hard to find and practically impossible to identify years later when they would simulate an interlobular septum or vascular sheath.

On many points I can offer no light: Why incipient organization is regularly snuffed out by resolution, but sometimes goes on to the full development of a permanent fatal lesion? What makes the exudate contract into plugs? Why fibrin favors the growth of fibroblasts? What are the origin, function and destiny of the various mononuclear

cells in pneumonic exudates? How the fibrogenic cells may be identified? and many others.

I believe, then, that pneumonic exudates organize by the metamorphosis into fibroblasts of cells originally exuded and that this change is favored by the presence of fibrin. I further believe that organizing pneumonia is the extreme development of a process which begins in a great many lobar pneumonias and is thus a sequel or complication of lobar pneumonia rather than a separate pathologic process.

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TWO CLASSIFICATIONS OF BRIGHT'S DISEASE*

ROLFE FLOYD, M.D.

IT is the object of this paper to compare briefly Delafield's classification of kidney diseases with that of Volhard and Fahr. Delafield, working first at Bellevue Hospital and later at Roosevelt in New York, at a time when autopsies could be performed on nearly every fatal case, published his classification in a series of papers about 1882, later compiled to form two volumes entitled "Studies in Pathological Anatomy." In later articles on the subject his original scheme was a little amplified but never radically changed, and his last publication, "Lectures on the Practice of Medicine with Cases and Charts," 1903, gives his final views, still essentially in agreement with those of 1882.

Volhard and Fahr, working at Mannheim in collaboration, the former on the clinical, the latter on the pathological side, published their classification in a volume entitled "Die Brightsche Nierenkrankheit" in 1914, again on the basis of autopsies on almost every fatal case.

About a generation separates these two pieces of work, each focuses the previous work done on the subject by others and each constitutes a notable achievement in itself; so their comparison is of interest.

First Delafield's views, then Volhard and Fahr's are given, each as nearly as possible in their own language. Then a comparison is drawn between the two conceptions.

1. DELAFIELD'S CLASSIFICATION. Delafield in his original article writes as follows:

Acute Bright's Disease. There is a general agreement, at the present time, that there is certainly one morbid condition to which the name of inflammation can properly be applied. This condition is characterized by an accumulation of blood in the vessels and an escape of the plasma, white

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cells and red cells from the vessels into the surrounding tissues. The inflammation is, therefore, called an exudative inflammation.

It may be that the congestion and escape of the elements of the blood from the vessels will be the only morbid change; or there may be added degeneration or death of the surrounding tissues, or a growth of new tissue. It is evident, in such an inflammation, that it is the blood vessels which are principally concerned. How and why it is that their walls are so changed that they allow the elements of the blood to pass through them we do not know, but the ordinary production of serum, fibrin, and pus in this way is a matter of everyday observation.

The introduction of certain poisons into the body is regularly followed by changes in the cells of the viscera. The poisons which exert this effect are ordinarily mineral poisons, such as arsenic, mercury, and phosphorus; or the poisons of infectious diseases, such as diphtheria, typhoid fever, etc. According to the quantity and virulence of the poison received into the body, there are more or less marked changes produced in the cells of the viscera.

Small doses of such poisons, acting only for a moderate length of time, produce a simple swelling of these cells. The cells are swollen, more opaque, more coarsely granular. They are not dead, nor broken down, nor do they contain any new substances; the change in their appearance is due to the swelling of the network which forms a part of every cell. Under these circumstances there are either no changes at all in the blood vessels of the viscera, or a slight congestion, with, perhaps, a little exudation of serum.

Larger doses of such poisons, or more virulent poisons, or a longer duration of the action of a poison, are attended by the deposition in the cell-bodies of granules of albuminous matter and globules of fat. At the same time there is a change in the nutrition of the cells, and they are often broken and disintegrated. Under these conditions there may be a considerable congestion of the vessels and an exudate of serum.

Very large doses of such poisons cause the death of the cells of the viscera, a death which may take the form of coagulation-necrosis or of disintegration and breaking-down

of the cells. With these changes there will often be an excessive congestion of the vessels and a large exudation of serum.

In many examples of acute exudative inflammation the only results of the inflammation are the inflammatory products and the death or degeneration of the tissues. Such an inflammation is regularly a transitory process; if it is not so severe as to cause death, it runs a limited course, the congestion subsides, the escape of the elements of the blood from the vessels ceases, and the tissues return to their natural condition. It may, however, happen that in an exudative inflammation there will be, from the very first, not only a production of serum, fibrin, and pus, but also a growth of new tissue. This new tissue, when once produced, is permanent and remains during the rest of the patient's life. Not only is this the case, but such an inflammation, instead of running a short and limited course, is apt to continue for months and years, with the continued production of more new tissue. The new tissue seems to originate in the connective tissue of the inflamed part. It is composed at first largely of cells, with but little basement substance; later it resembles more closely ordinary connective tissue. Such an inflammation may be called "productive" or "diffuse" inflammation.

The three morbid conditions just described are the morbid conditions which affect the kidneys in acute Bright's disease. All the cases of this disease are examples of an acute exudative inflammation, or of an acute degeneration, or of an acute or subacute diffuse inflammation.

We divide acute Bright's disease, therefore, into three classes and describe:

Acute Exudative Nephritis: Acute Degeneration of the kidney; Acute Diffuse Nephritis. [To these Delafield subsequently added Acute Congestion.]

Chronic Bright's Disease. The chronic forms of Bright's disease are of much more frequent occurrence than are the acute forms. The cases of the disease are very numerous, they present a good deal of variety in their lesions and in their symptoms, but they can all be conveniently grouped under the three heads: Chronic Congestion of the Kidney; Chronic Degeneration of the Kidney; Chronic Diffuse Nephritis.

"Diffuse" here means with growth of new interstitial tissue. Here then are seven conditions which are defined as follows:

1. Acute Congestion, a temporary congestion of the blood vessels of the kidney which may be accompanied with exudation of serum and escape of red blood-cells. Causes: cantharides and turpentine, extirpation of one kidney, severe injuries, surgical operations especially on the genitourinary system.

The cardinal symptom is diminished urine with albumin, casts, and blood cells in it, or complete suppression which may be fatal. Recovery is the rule.

2. Acute Degeneration of the Kidneys. An acute change in the kidneys, characterized by degeneration or death of the epithelial cells of the tubules to which may be added an exudation from the blood vessels. Causes: mercury, arsenic, phosphorus, poisons of infectious diseases, etc. The lesion varies according to the quantity and violence of the poison.

The changes in the renal epithelial cells are: a simple swelling of the cell-body, causing it to look larger and more opaque and to take on irregular shapes; an infiltration of the cell-bodies with granules of albuminoid matter and fat; a death of the cells, which may take the form of coagulation necrosis or of a disintegration of the cell-bodies; a desquamation of the dead cells so that the tubes are filled with them; a formation of hyaline masses in the cells; a growth of new cells to take the place of the dead epithelium. All these changes are most marked in the convoluted tubes. In the kidneys with extensive necrosis of the epithelium there may also be congestion of the blood vessels and casts in the tubes.

Symptoms. With the severe acute degeneration which follows the ingestion of large doses of arsenic, mercury, or one of the other inorganic poisons, the urine is diminished in quantity, or suppressed; it contains albumin, casts, and blood; its specific gravity is unchanged. At first the general symptoms belonging to the poison predominate, but as these subside the patients continue to live and suffer more or less severely from the degeneration of the kidney. They become feeble, pass into the typhoid state, and often die.

The acute degeneration which accompanies the infectious diseases such as scarlatina, diphtheria, typhoid fever,

pneumonia, etc., is for the most part of mild type and gives no symptoms except the presence of a little albumin and a few casts in the urine. It is of importance to recognize the frequency with which this affection of the kidney occurs, the slight injury which it inflicts on the patient, and the completeness with which the kidney lesion disappears after the recovery from the primary disease. Much unnecessary anxiety is often felt by physicians because in a case of pneumonia or some other infectious disease they find albumin and casts in the urine. There are fears not only of death from the primary disease, but of the subsequent development of "Bright's disease." If the albumin and casts are due to degeneration of the kidneys, anxiety is needless. The course of the primary disease will not be changed. If the patients recover their kidneys return to their normal condition.

With yellow fever, with acute yellow atrophy of the liver, and occasionally with the other infectious diseases the degeneration is of intense type, with the death of a large part of the renal epithelium and exudation from the vessels. In such cases the urine is scanty or suppressed. It contains albumin, casts, and blood. The patients are very ill, they may have convulsions, delirium, or stupor; they often die. But it is hard to tell how many of their symptoms are due to the complicating kidney lesion.

3. *Acute Exudative Nephritis.* An acute inflammation of the kidneys characterized by congestion, exudation of the blood plasma, emigration of white blood cells, diapedisis of red cells, to which may be added changes in the renal epithelium and glomeruli. Causes: primary or secondary to any infectious disease, especially scarlet fever; occurs also with pregnancy.

In a nephritis of this type we should expect that the inflammatory product, the serum, white and red blood cells, and coagulable matter from the blood plasma, would collect in the Malpighian bodies and tubes, or infiltrate the stroma between the tubes; and that of the inflammatory products in the tubes and Malpighian bodies a part would be discharged with the urine and a part be found in the kidney after death. We should also expect that the quantity of inflammatory products would be in proportion to the severity

of the inflammation, and that an excessive number of pus-cells would belong to the especially severe forms of the disease. Still further, it is evident that with the milder examples of nephritis, with but little exudation, no inflammatory products might be found in the kidney after death, all having been discharged into the urine during life. As a matter of fact, the kidneys do present just such changes. When the patient recovers the kidneys return entirely to normal.

These cases show large amounts of albumin and casts and blood, subcutaneous dropsy, increased blood pressure, gastrointestinal and cerebral symptoms, and convulsions. They may be so mild as to be overlooked. They regularly recover unless death occurs with anuria or other severe symptoms early in the disease. They do not become chronic.

There is a special form with an exudate of pus either in the tubes or in the stroma which is very fatal.

4. *Acute Productive Nephritis.* An acute inflammation of the kidneys, characterized by exudation from the blood vessels, a growth of new connective tissue in the stroma and changes in the epithelium and glomeruli.

This is the most serious and important of the forms of acute nephritis, for the reason that its lesions are from the first of a permanent character. It does not follow exudative nephritis, nor is it merely a modification of it; from the very onset it is a different form of inflammation. In the kidneys of persons who have been sick only a few days the characteristic lesions are already evident.

To the lesions seen in acute exudative, two more are added: (1) a growth of new connective tissue in all, often in wedges; (2) a development of the capsule cells of the glomeruli to form "half moons" in some. The kidney never can return to normal for the stroma and glomerular changes persist. Apparent recoveries are apt to be followed years later by further kidney disease.

The onset may be acute or subacute and the course is longer than in the exudative type. The dropsy involves the serous cavities as well as the skin.

5. *Chronic Congestion.* A persistent overfilling of the kidney capillaries and veins with blood due to some obstruc-

tion of the circulation such as valvular disease, myocardial weakness, aortic aneurysm, pleural effusion. The glomeruli show the most constant and characteristic change, their loops being thickened and dilated; the epithelium of the tubes is flattened, or it is swollen and its individual cells separated from each other. The pyramidal veins are dilated. There is no growth of new connective tissue. There are no renal symptoms. The urine is small in amount, of high gravity and contains a little albumin and a few casts. The importance of the condition is that it may lead to a chronic nephritis.

6. *Chronic Degeneration of the Kidney*, characterized by degenerative changes in the renal epithelium caused by the same circulatory disturbances which produce chronic congestion, by chronic wasting diseases, such as phthisis and cancer, and in some cases occurring primarily without known cause. The renal epithelium is swollen and coarsely granular but there are no changes in stroma, arteries or glomeruli. The urine shows little albumin; neither dropsy, increased blood pressure nor cardiac hypertrophy occur. The importance of the condition is that it may lead to chronic nephritis. The rare primary cases are difficult to diagnose. They may be the cause of death from inanition.

7. *Chronic Nephritis.* A chronic inflammation of the kidney attended with a growth of new connective tissue in the stroma, permanent changes in the glomeruli, degeneration of the renal epithelium, and sometimes changes in the walls of the arteries. It has been customary to hold that in one set of these kidneys the primary and most important changes are in the renal epithelium, while in another set of kidneys the primary and important changes are in the stroma.

In other words, that the cases of chronic nephritis can be divided into two classes, parenchymatous nephritis and interstitial nephritis. I do not think that this classification is supported by facts.

In all the forms of chronic nephritis changes are to be found in the renal epithelium, the glomeruli, and the stroma. Whether the changes in the stroma, the glomeruli, or the epithelium are the more marked makes no difference in the clinical symptoms. But the presence or absence of exudation from the renal blood vessels does correspond to a marked

difference in the symptoms. The existence of the exudation from the renal vessels is easily shown by the presence of serum albumin in the urine. In this way we readily distinguish two forms of chronic nephritis, one with exudation and one without.

The way of looking at the matter, then, is this: we find after death from chronic nephritis a great many varieties in the gross appearance of the kidneys. Some are large, some are small, some are red, some are white, etc. There is no regular correspondence between these different gross appearances of the kidneys and the clinical symptoms.

We find in these same kidneys changes in the renal epithelium, in the stroma, in the glomeruli, and in the arteries. Sometimes one, sometimes another of these elements of the kidneys is the most changed. There is no regular correspondence between the predominance of the changes in one of the kidney elements over the other and the clinical symptoms.

The easiest working scheme is to admit that in chronic nephritis all the elements of the kidney are more or less changed, but that the cases vary as to whether there is or is not an exudation of serum from the blood vessels. The presence or absence of such an exudation does correspond to a well-marked difference in the clinical symptoms. In the present state of our knowledge and for clinical purposes, we divide all the cases of chronic nephritis into two classes; chronic nephritis with exudation and chronic nephritis without exudation. It is admitted that it is easy to divide up these kidneys according to their anatomical changes, into a number of fairly well-marked classes. But as this division does not correspond to clinical divisions it is valueless for clinical purposes.

Although it is convenient to describe two forms of chronic nephritis—one with much albuminuria and dropsy, and one with little or no albuminuria or dropsy, yet it must be remembered that these are not separate lesions of the kidneys, but varieties of the same lesion. For in all these kidneys two changes are constant—productive inflammation of the glomeruli and stroma, and degeneration of the renal epithelium. The only real difference between the kidneys is whether, besides the growth of new tissue and degeneration

of renal epithelium, there is or is not an exudation of serum from the blood vessels of the kidneys.'

A considerable number of cases of chronic nephritis follow an attack of acute or subacute productive nephritis. The conditions of chronic congestion and chronic degeneration of the kidney are not infrequently followed by a true nephritis. Syphilis, chronic tuberculous inflammation of any part of the body, chronic endocarditis, and chronic suppurative inflammations are often complicated with chronic nephritis. It is very difficult to find a satisfactory cause for the primary cases. There are many of these, especially in young and middle-aged adults. The nephritis is developed in a slow, insidious way in persons whose previous health has been good, and in whom no exciting cause is discoverable.

(*A*) *Chronic Nephritis with Exudation.* Symptoms: Urine reduced in acute exacerbations, increased in later stages, even up to 100 ounces a day. Specific gravity of the urine and percentage of urea gradually fall. Albumin and casts vary in amount with the activity of the inflammation, in general they correspond to the dropsy.

Secondary anemia with a peculiar pallor is a very constant feature. Dropsy is almost a constant symptom, for it forms the basis of the clinical classification. Increase of blood pressure may be present or not, and cardiac hypertrophy also is usual but not constant. Chronic uremia with alternating delirium and stupor is an ordinary mode of death. Albuminuric retinitis may occur at any stage and is of bad prognosis. Dyspnea is a nearly constant symptom but arises in various ways: hydrothorax, edema of the lungs, contraction of the vessels, failing heart. Anorexia and vomiting are very frequent. There is hardly any limit to the variations of the disease but the "most constant symptoms are anemia, dropsy and albumin in the urine."

(*B*) *Chronic Nephritis without Exudation.* This form belongs more to people over forty-five and is apt to be associated with chronic inflammation of other organs. The symptoms differ from those in the above type in the following ways: albumin and casts are less constant and less in amount; dropsy is usually absent and more dependent on circulatory difficulties; acute uremia, dependent on vascular contraction,

is more frequent than chronic uremia. The symptoms due to complications, such as cardiac hypertrophy and valvular lesions, arteritis, and emphysema, are more frequent and more prominent.

11. Volhard and Fahr's Classification. Volhard and Fahr approach the subject as follows:

Pathogenesis and Classification. The chief difficulty in a classification of Bright's that corresponds at once to pathological and clinical observations is that there is no agreement about the pathogenesis of the various forms.

At Meran in 1905 the pathologists expressed a certain resignation in this matter and the clinicians were even less able to lead the way to a common viewpoint. Since then the clinicians have spoken loudly, questioning the possibility and also the necessity of such a unifying comprehension, a position which evidences a similar resignation on their part.

And still it seems to us that an agreement about the pathogenesis and a consequent pathogenetic classification is possible. Such an one has gradually developed for us in our work together as pathologist and clinician and is finally to be here presented.

With the greatest esteem for biological criticism and recognition of the importance of the principle of judging aberrations of normal function by functional standards, our ultimate objective is to bring clinical symptoms into correspondence with pathological findings; not so much for the purpose of standing the test of pathological anatomy, as from the necessity of understanding the abnormal functions, that is, in the final analysis, in order to be able to refer them back to pathological processes, to cellular changes, or definite chemical products of diseased-cell activity.

A functional classification must not, under the pretext that functional changes have nothing to do with the microscope, lead away from pathological anatomy. On the contrary it should lead to increasing cooperation with and dependence on pathology, and the failure of a histological method only demands further perfecting of technique but gives no license for any but an anatomical interpretation of disordered function.

For the sake of being better understood I shall begin with the generally used, though completely useless division into parenchymatous and interstitial forms. We have found that neither of these forms represents a pathogenetic unit.

The proper clinical criteria for classification are blood pressure and kidney function. We have found with the same "parenchymatous picture" two types, one with blood pressure and one without, and among the "interstitial" high tension cases again two types, differentiated by presence or absence of failing kidney function.

1. The so-called parenchymatous, nonindurative forms. Here the blood pressure is the important classifying feature, for it has been found to correspond to an anatomical difference. In the gross "large white kidneys" are found both without and with increased blood pressure and this has led to the false conclusion that large white kidneys were all the same lesion and the blood pressure an unessential complication. When the blood pressure fails, so do the evidences of inflammation, viz., hyperemia, stasis, exudation, proliferation. In this group degeneration of the epithelium is the essential change, the stroma and blood vessel changes sinking far into the background, though when fully established they do show leucocyte infiltration as well as stroma increase. Unquestionably these inflammatory changes, because of their meagerness and their absence in fresh cases, are to be regarded as secondary and stimulated, as Weigert interprets them, by the products of cell degeneration and as a replacement fibrosis that finally reaches a large diffuse development and may lead to contraction.

If now we turn to inflammation and its primary vascular changes it is evident that these must be present in, and characterize, any true nephritis. The degeneration cases in which inflammatory changes fail can then be called nephrosis in contradistinction to the inflammatory ones.

The etiology of primary degeneration types or nephrosis cases without increased blood pressure is unknown, but it is characteristic that they cannot be referred to any of the known agents that injure the kidney.

The evidences of nephritis are blood pressure and blood in the urine, and, under the microscope, an inflammation of the

glomeruli as well as the extensive epithelial degeneration, which is common to both types of large white kidney and on which extensive dropsy chiefly depends. As a rule the damage to the epithelium is an anemic degeneration, the result of the glomerulitis, the inflammation of the vessels, occlusion of the capillary loops, and stopping of the blood stream and of the oxygen supply. In some cases, however, the severity of the epithelial changes are out of all proportion to the glomerulitis, both in extent and degree, and such cases we regard as mixed forms, when nephrosis and nephritis coexist, probably due to a common poison.

We believe that increased blood pressure depends (except in cases of anuria) on diffuse involvement of the kidney vessels and that dropsy, on the other hand, is induced by changes in the tubular epithelium, a constant lesion in simple nephrosis, but also a frequent complication in nephritis.

The waxy kidney has been described as a separate type of disease, but it has been noted how often it gives the clinical picture of nephrosis without cardiac hypertrophy, retinitis and uremia.

We do not believe that a typical amyloid kidney can be differentiated from nephrosis without amyloid. We therefore regard it as an unessential complication of nephrosis and regard both the epithelial and vascular changes as due to the same cause. The same conclusion holds for the contracted nephrotic kidney with and without amyloid. Amyloid changes in no way alter the symptoms. For these reasons the amyloid kidney as a separate entity is omitted from the classification.

Though increased blood pressure never occurs in nephrosis it may also fail in some forms of nephritis, viz., embolic focal nephritis, interstitial focal nephritis, and focal glomerulonephritis. The focal cases bespeak a bacterial infection, rather than a soluble toxin as the causative agent. Rise in blood pressure thus differentiates diffuse and focal nephritis and the blood pressure is to be referred to the diffuse or general involvement of the glomeruli; that is to say, of the vessels.

The differentiation of nephrosis from focal nephritis depends on large amounts of dropsy and albumin in the former and hematuria in the latter.

The terms acute, subacute, and chronic are not good for classification, but useful in denoting stages of each type. They indicate prognosis, stage, duration, onset, and course. Chronic usually means not curable, but this does not apply strictly to nephrosis.

11. *The "Interstitial" or Indurative Form.* The classical symptoms of these are cardiac hypertrophy and high blood pressure. These we have divided by a study of renal function into a benign group with good function and a serious group with failing function.

(*a*) The group with good function includes the "red atrophic" or "red granular" kidney, and also its developmental stages, in which there is no contraction and often no granulation. New connective tissue may or may not be present, varying numbers of glomeruli are diseased, but all these cases of the benign group have two common features: (1) elastic proliferation of the intima of the kidney vessels; (2) absence of degeneration of the uninvolved parenchyma and of any considerable inflammatory reaction. The patient behaves as a simple cardiac with arterial symptoms referable to kidney, heart, brain, or peripheral vessels, depending on the location of the lesions.

(*b*) The second differs from the first in exhibiting renal insufficiency and shows a secondary contracted kidney, the scarring stage of an inflammatory process with extensive parenchymal changes. In early stages the contraction may be slight or lacking. "Secondary" may be applied also to contraction after nephrosis, and after diffuse and focal glomerulonephritis.

These cases show very high blood pressure and cardiac symptoms combined with renal insufficiency and, histologically, marked arteritis of the small and smallest vessels with an inflammatory glomerular change: a combination form. The smallest vessels are more often involved in this form than in the simple sclerosis. This may be the predisposing cause of the parenchymal changes. In any case in the combination forms the vascular change is primary and older; the inflammatory or parenchymal more recent and secondary. A group of "contracted kidney" is impracticable because contraction cannot be diagnosed in life. The dis-

turbance of renal function is the important feature, and this depends on destruction of parenchymal secretory tissue quite independent of the degree of contraction, so we prefer to call these cases of hyposthenuria and failing renal function "End stages."

We do not base our classification upon etiology because in part of the cases it is unknown and in another set it is the same for all.

The pathological significance of four cardinal symptoms in these conditions is then as follows:

(1) Dropsy depends on degeneration of the epithelium of the convoluted tubules.

(2) Hematuria depends on inflammation of the kidney especially expressed in glomerular and interstitial lesions.

(3) A large amount of urine of low and constant gravity (hyposthenuria) indicates a failure of renal function and an extensive destruction of secretory renal tissue.

(4) High blood pressure and cardiac hypertrophy depend on arteriosclerosis of the renal vessels (in so far as they depend on the kidney at all).

Two tabulated classifications are given in the work, one by Fahr in the pathological portion, the second by Volhard in the clinical section. That of Volhard is here given, slightly amplified in detail to include all that appears in Fahr's scheme.

PATHOGENIC CLASSIFICATION OF BRIGHT'S DISEASE

A. Degenerations, affecting principally the tubular epithelium. Nephrosis.
   1. Genuine simple nephrosis of unknown origin. Four stages, viz., (*a*) cloudy swelling, (*b*) epithelial degeneration, (*c*) growth of interstitial tissue (*d*) nephrotic contracted kidney with failing function, but no increase of blood pressure.
   2. Secondary simple nephrosis of known origin. Above stages not so distinctly developed.
   3. Characteristic nephrosis; presenting, in addition to common features, lesions peculiar to a special poison.

4. Necrotizing nephrosis, with death of epithelium. [A lesion may be at once "characteristic" and "necrotizing," as the bichloride kidney, and thus belong at once to 3 and 4.]
5. Complicated nephrosis; the amyloid kidney. Three stages correspond to last three of simple nephrosis.

B. Inflammations, affecting chiefly glomeruli and stroma. Nephritis.
1. Diffuse glomerulonephritis with increased blood pressure. ["Diffuse" here means that all the glomeruli are inflamed.] Three stages, viz., acute, chronic, and end stage with failing renal function.
2. Focal nephritis without increased blood pressure. (*a*) Focal glomerulonephritis, acute and chronic stages, (*b*) septic interstitial focal nephritis, (*c*) embolic focal nephritis.
3. Mixed forms of nephritis and nephrosis.

C. Arteriosclerosis—affecting primarily the renal vessels—always associated with hypertension.
1. Simple sclerosis.
2. Combination form, sclerosis plus nephritis, true contracting kidney with rapidly fatal course.

A. Nephrosis comprises all purely degenerative lesions and those whose inflammatory nature is not entirely beyond question. They are caused by poisons, either bacterial, mineral, or metabolic, and sometimes they arise without known cause and are then termed genuine.
1. Genuine nephrosis occurs in four stages.
   (*a*) Cloudy swelling, in which the cells are enlarged and the Altmann granules are irregular in disposition and various in size. Glomeruli and stroma normal. This causes no symptoms except a trace of albumin and a few casts. It is very common and occurs as an incident in many infections.
   (*b*) Epithelial degeneration, in which hyaline droplets and fat collect in the cells and some nuclei disappear. Glomeruli and stroma normal. This occurs under the same circumstances as cloudy swelling, causes no more symptoms, and like it, vanishes

completely as the primary infection subsides. It also may produce the fully developed clinical picture of nephrosis with dropsy and much albumin in the urine, which occurs either in early amyloid kidney, in genuine nephrosis, or in the large white kidney with hypertension which we call the "mixed form."

(*c*) Inflammatory reaction in vasculo-connective tissue, in addition to epithelial degeneration. There is a definite growth of new interstitial tissue, some desquamation of the epithelium of the convoluted tubes, some dilatation of the tubes, and rarely some regenerating epithelium. Glomeruli are normal. [These observations are based on only two cases, all that the authors have seen at autopsy.] In these the complete clinical picture of nephrosis occurs. Marked oedema of skin and serous cavities due to permeability of the vessel walls is the most striking symptom. The transudates are milky and poor in albumin. Urine of very high gravity, small in amount, and containing large amounts of albumin and many casts and fatty cells, but seldom any red cells. Blood shows no anemia in spite of the pale skin, the serum is milky, like the transudates. Rest nitrogen is never much increased, values of 80 mg. are infrequent, and 100 mg. was only seen shortly before death or with anuria incidental to a complication.

True uremia due to failure of the excretory renal function never occurs.

Anorexia and watery diarrhea are regular symptoms. The absence of increased blood pressure and of cardiac hypertrophy are characteristic. "We only saw them when renal arteriosclerosis was present in addition." Eye ground changes are never observed.

(*d*) Cicatrization with destruction of both tubes and glomeruli by the contraction of the inflammatory interstitial tissue. A few glomeruli pri-

marily inflamed. Tubal epithelium degenerated and sometimes regenerating. [This description based on one autopsy in a man dying of phthisis.] With this lesion there is polyuria and loss of urinary concentrating power, but no rest nitrogen retention and no increased blood pressure, cardiac hypertrophy, retinitis, or uremia.

The course of nephrosis is slow and discouraging: first a period of very marked general edema, then one when the edema is confined to the serous cavities, then a period with albuminuria without edema, haematuria, or increase of blood pressure, and finally, unless they get well before, a final stage of hyposthenuria without increase of rest nitrogen or hypertension.

2. Secondary simple nephrosis with known cause, essentially similar to 1, but stages are less distinct both as to lesions and symptoms.
3. Characteristic nephrosis, in which some special added feature occurs with some particular causative agent, thus lime deposit and regenerating epithelium in bichloride kidneys or glycogen deposits in diabetes.
4. Necrotizing nephrosis. The epithelium of the convoluted tubes is extensively necrotic, the glomeruli are normal. Bichloride given as an example.
5. Complicated nephrosis. The amyloid kidney. The authors consider this lesion nothing more than an ordinary nephrosis of known cause, in which waxy deposits occur. The amyloid, unless in large amounts, produces no modifications in the symptoms. This nephrosis may show simple epithelial degeneration or an interstitial growth of new tissue in addition, which latter may pass on into a condition of cicatrical contraction. The symptoms are those of simple nephrosis.

B. Inflammations. Nephritis, in sharp contrast to nephrosis. The damaging poison in nephritis produces, from the beginning of the process, strictly inflammatory changes in the glomeruli and in the interstitial tissue. The heart and the vessels are involved in the later stage.

1. Diffuse glomerulonephritis. ["Diffuse" here meaning that practically all the glomeruli in both kidneys are inflamed, while Delafield uses the same adjective in quite another sense, namely, to mean that the stroma is involved in the inflammatory process.]

This is caused by streptococci, pneumococci and by tuberculosis. It is especially apt to follow angina.

(*a*) Acute stage.

The glomerular lesion dominates the picture and establishes the diagnosis. This consists in a multiplication of the glomerular cells and an elongation and dilatation of the vascular loops. The increase of cells chiefly concerns those within the loops, polynuclears and endothelium, but a swelling, increase, and degeneration of the tuft epithelium occurs also. An exudate of red, white, and epithelial cells and of albumin appears within the glomerular cavity. There is little blood in the capillary loops.

Degenerative changes in the epithelium of the convoluted tubes as described in nephrosis is the rule, but varies greatly in amount. Casts, red blood cells, and coagulated albumin occur in the tubes.

There are a few small round cell infiltrations in the interstitial tissue. This condition often returns entirely to normal.

(*b*) Chronic stage shows more advanced glomerular and epithelial lesions and, especially, increased inflammatory reaction in the institial tissue.

The glomerular lesion may be that of the acute stage, intracapillary, or there may be in addition an extensive ingrowth of the capsular epithelium which compresses the tuft; "extra capillary" or "half-moon form." The latter belongs to the severest cases.

(*c*) End stage—with profound alteration of kidney architecture through production and contraction of interstitial tissue; many tubes and glomeruli damaged beyond the possibility of functioning,

others showing a compensatory dilatation and hypertrophy.

Clinically hypertension typifies the condition, though hypertension also occurs with arteriosclerosis, and with the anuria of bichloride kidneys. It is absent if the inflammation is focal instead of diffuse, in very mild cases, and in high fever and profound general weakness. Edema is very usual, but not constant; when excessive it indicates a degeneration of the tubal epithelium. Cardiac hypertrophy is the rule. Presence of blood in the urine is the surest sign of nephritis. Albumin and casts are nearly constant. Renal function and rest nitrogen are normal in the acute and chronic stages, but the end stage is marked by progressive renal failure. Such failure can supervene early, especially with the "extra capillary" lesion. Eye-ground changes belong to the end stage.

Many cases recover after the acute stage, some go on into the chronic often with few symptoms, and most of these sooner or later come to a failure of renal function and the end stage which results in fatal uremia, unless death from some intercurrent condition, especially heart failure, anticipates it.

2. Focal nephritis, in which the lesion is not diffuse, but developed in foci, or patches, the intervening renal tissue remaining normal.
   (*a*) Focal glomerulonephritis. Same lesion as diffuse, but not so extensively developed. Clinically evidenced by hematuria without increased blood pressure, dropsy, or increased rest nitrogen. Not a fatal condition, so this lesion is seldom seen. Probable that it can develop into a diffuse lesion with resulting changes in symptoms.
   (*b*) Septic interstitial focal nephritis. The lesion consists of foci of round, plasma, and a few pus cells in the stroma, without glomerular or other changes. This gives no symptoms,

even albumin is absent from the urine, or only occurs in traces. It forms part of a general sepsis; renal symptoms only become prominent if anuria supervenes.

(*c*) Embolic focal nephritis. The ordinary septic emboli that occur with an infectious endocarditis.

C. Sclerosis—primary lesions of the renal arterioles.

1. Simple sclerosis. A new growth of elastic lamellae in the intima, hypertrophy of the muscle coat, degeneration of the new elastic tissue, fatty degeneration, atrophy and replacement fibrosis in the muscle coat.

   The cause is unknown, but it belongs to adults over fifty. Increased blood pressure averaging 200, and cardiac hypertrophy without hematuria, with little or no albumin, without any increase of rest nitrogen, and without neuroretinitis, make up the clinical picture. Arteriosclerosis of the heart and of the brain often complicate it.

   This disease often causes no symptoms for long periods, and runs a chronic course, but always with the possibility of fatal arterial attacks.

2. Combination form. A sclerosis like the last but always involving the smallest renal arterioles, which is subsequently complicated by progressive inflammation of the glomeruli and interstitial tissue, finally leading to a destruction of secretory tissue so extensive as to cause failure of renal function.

   As soon as this complicating inflammation develops the chronic course changes to a rapidly unfavorable one, albuminuria appears, the blood pressure rises, averaging 240, the heart becomes enormously enlarged, and tends to fail, arterial symptoms become aggravated, loss of flesh and strength is rapid, secondary anemia and cerebral symptoms appear, rest nitrogen accumulates and fatal uremia is the necessary conclusion. Neuroretinitis is especially typical of the condition and often appears before any other symptom.

Comparison of the Two Classifications. Both these classifications constitute a determined attempt to interpret

renal symptoms in terms of renal lesions, which is the basis of their strength.

Both differentiate between degenerative changes in the tubular epithelium and inflammation of the organs as a whole.

Both consider the ubiquitous division of kidney cases into parenchymatous and interstitial as useless, invalid and misleading.

Both Delafield and Fahr describe almost precisely the same microscopic lesions of glomeruli, tubes, stroma and blood vessels, although their comprehensions of the pathogenesis and clinical significance of the varying combinations of these individual lesions differ, at times widely.

Volhard and Fahr have the advantage of more various and refined histological methods and of all the recent methods of studying renal function, hypertension, etc., an advantage which they improve to capacity. It is a little surprising that, in the matter of illustration, while their colored plates are excellent, they cannot compare with the microphotographs of Delafield's original work.

Delafield describes acute and chronic congestion as distinct pathological and clinical entities. Acute causes diminished urine or anuria, which leads him to the belief that diminished and suppressed urine in acute nephritis and in exacerbations of chronic are due to the concomitant acute congestion. Chronic congestion causes a definite dilatation and thickening of the glomerular loops but no changes in the stroma. It causes only minor clinical manifestations, but is important because it may be followed by a chronic nephritis, with the growth of cells in the altered glomerular loops and of new interstitial tissue.

Volhard and Fahr do not describe either of these conditions. They repeatedly describe the anuria of acute inflammation, but do not attribute it to congestion. They refer to the chronic congestion incident to cardiac difficulties, but do not describe the lesions and nowhere indicate that it may lead to a chronic nephritis. I have among Delafield's own slides excellent specimens of these glomeruli of chronic congestion, both before and after the incidence of the inflammatory cell growth, and there can be no question as to the lesions he describes.

Although in the degenerative changes the lesions described by both Delafield and Fahr are practically the same, it is here that the widest divergence in the conception of their pathological development and clinical significance occurs.

Both have seen cloudy swelling, vacuoles and fatty deposits in the renal epithelium without glomerular changes as an incident in all sorts of infectious diseases and causing no symptoms or only a trace of albumin and a few casts in the urine.

Both have seen necrosis of the renal epithelium with mineral poisons, and Delafield has seen it in yellow fever and acute yellow atrophy as well.

Both have seen young people with dropsy, large amounts of albumin and casts, and pallor and prostration, without hypertension or cardiac hypertrophy, and found a large white kidney with extensive fatty and degenerative changes in the epithelium, new cell growth in the interstitial tissue, and little change in the glomeruli.

Both have seen the same clinical picture, but with hypertension and a big heart combined with a similar pathological picture, in which Volhard and Fahr, however, see more glomerular changes.

Both have seen waxy kidneys, with new cell growth in the stroma and much albumin and dropsy, accompanying wasting diseases.

For Delafield, cloudy swelling, vacuoles, and fatty infiltration in the cytoplasm, failing nuclear stain, desquamation and wholesale necrosis of the cells are simply steps in one process whose severity depends on the degree of the poison. Regenerating epithelium he saw and described in bichloride. Necrosis he saw after mercury, arsenic, phosphorus, yellow fever, and acute yellow atrophy of the liver. In many cases, especially the more pronounced, a minor inflammatory reaction occurs in conjunction, but no glomerular or interstitial changes.

Clinically he found only traces of albumin and granular casts, except in the necrotic forms, and in none of them did he ever see dropsy.

For Delafield a kidney with definite new cell growth in the stroma, in addition to changes in tubes and glomeruli,

without or with cardiac hypertrophy and hypertension, is a case of chronic nephritis.

Waxy kidneys, also, according to Delafield's conception just given, are a special type of chronic nephritis.

Volhard and Fahr have seen cloudy swelling, hyaline deposits, and fatty deposits and some loss of nuclei, with traces of albumin, a few casts, and no dropsy, as an incident in many infections. They assume, however, that hyalin droplets and fatty deposits and fading nuclei, with no other changes—in other words, a pure degenerative lesion—can cause large amounts of albumin in the urine and extensive dropsy, but they have never seen such a case at autopsy, at least they do not report any.

It is just here that Delafield has the advantage of them, for he has seen many cases of pure chronic degeneration at autopsy, some incident to heart disease and stasis, some to chronic wasting diseases, and some arising primarily and constituting the only important lesion at autopsy. In no such case did he see more than a trace of albumin or any renal dropsy.

Volhard and Fahr, perhaps because they have not seen such autopsies, consider kidneys with much degenerated epithelium, a growth of new interstitial tissue, and absence of hypertension and of cardiac hypertrophy the normal outcome or later stages of cloudy swelling, cytoplasmic degeneration and fading nuclei. They have seen only 3 such at autopsy.

Although, as above stated, they have seen these degeneration changes with acute infections repeatedly without dropsy (p. 148), they yet regard the epithelial degeneration as the cause of pronounced albuminuria and of dropsy, not only in all this group which they call nephrosis, but also when associated with definite inflammation, glomerular and interstitial lesions and hypertension.

They further consider necrosis of the epithelium an aberrant form of degeneration instead of the natural final stage of the degenerative process, even in spite of having seen transitional lesions with early and partial necrosis.

In waxy kidneys they regard the epithelial degeneration as the one important change and the cause of albuminuria and dropsy, and regard the amyloid deposits, interstitial,

and glomerular changes as comparatively negligible. The occasional hypertension they refer to complicating renal arteriosclerosis.

I have tried to state their view fairly, the more because I disagree with it. It appears unsound, for the reasons: (1) its autopsy support is altogether inadequate; (2) renal dropsy has not been shown to occur with epithelial degeneration alone; and (3) in other organs, such as the nose, colon, etc., large exudates of albuminous fluid have not been shown to be primarily dependent on epithelial degeneration.

Turning now to the inflammations, we find similar fundamental conceptions of the process; namely, that the blood vessels are always concerned, that exudation of blood elements is an essential part of it, and that new cell growth in the stroma may or may not occur. Practically, however, the two views present differences.

Volhard and Fahr regard glomerular inflammation as the pivotal fact in all nephritis, except a rare septic interstitial form and the cases with septic emboli that accompany infectious endocarditis. The two main questions for them are: (1) whether all the glomeruli or only part of them are diseased, and (2) whether the inflammation is of the intra- or extracapillary type. Only in diffuse glomerulonephritis, i. e., where all the glomeruli suffer, are renal symptoms developed to any extent. The extracapillary form is much the severer, but only appears late in the course of cases which have not been properly treated in the acute stages. In their opinion no acute case of nephritis should become chronic if properly treated.

Delafield, on the contrary, draws a sharp distinction between two types of acute nephritis. In one, acute exudative nephritis, the inflammatory process consists of exudation of the elements of the blood, with or without glomerular changes and degeneration of epithelium. Recovery occurs in almost all, and with recovery the kidney returns entirely to normal. In the other, acute productive nephritis, in addition to the above changes, there is a growth of interstitial tissue from the outset, and the glomeruli are invariably altered. This lesion always leaves permanent damage. Delafield shows a microphotograph of such a kidney on the sixth day after acute

onset of symptoms. These cases also often show the "extra-capillary" type of glomerular inflammation from the outset, a fact which Volhard and Fahr fail to recognize. Altogether, Delafield's comprehension of acute nephritis is the more adequate and corresponds better to clinical experience.

It is interesting to note, in passing, that both observers recognize a rare acute septic form with a large exudate of pus in the interstitial tissue and unassociated with much albumin in the urine. Delafield also saw cases of the same kind but with the pus in the tubules, so he called the condition acute exudative nephritis with pus cells, while Volhard and Fahr, having seen only the interstitial type, call it septic interstitial focal nephritis.

When it comes to chronic nephritis, Delafield recognized the various lesions and also insisted on the fact that in every chronic case showing renal symptoms, such as dyspnea, dropsy, hypertension and hypertrophy, uremia, and so on, the changes in the secretory tissues were invariably accompanied by changes in the stroma, so that, for him, the absence of such stroma changes meant that the case was not one of chronic nephritis. Delafield, however, frankly confesses his inability to cope successfully with the classification of chronic nephritis.

It is this group, especially, that Volhard and Fahr attempt to analyze and subdivide. In the first place, they take out the cases with dropsy and albumin, but without hypertension, and call them nephrosis, a move that has already been discussed. Next they divide chronic nephritis into a chronic stage with good renal function and an end stage where this fails, unquestionably a valid and helpful distinction. Also the division of uremic symptoms into those due to failure of renal excretion (true uremia), to edema of the brain (eclamptic uremia), and to spasm of the cerebral vessels (pseudouremia) is most enlightening and suggestive. In fact, the study of renal function as a whole with the results of various functional tests is a most excellent and valuable contribution and would, in itself, be enough to entitle the work to the highest consideration.

Finally they separate all the cases whose primary lesion is in the arterial walls, calling them sclerosis, and divide

them, as above indicated, into simple forms, and those followed by a secondary inflammatory change in the secretory tissue not directly compromised by the sclerotic process. All the scleroses, except the earliest, having a stroma change, fall in Delafield's chronic nephritis group. In support of their views concerning sclerosis, Volhard and Fahr cite numerous cases with autopsies and, to my mind, present a very strong and convincing argument. If their conception of renal sclerosis proves correct, as it promises, it is destined to amplify greatly our knowledge of a dark and difficult subject.

There is a joint in the armor, however, which, though it does not invalidate the sclerosis group, confuses their presentation of nephritis; and to this I wish to draw attention.

Just as they look at degeneration of epithelium as the cause of renal dropsy and albuminuria, so they regard sclerosis as the cause of renal hypertension. They state, however that hypertension is an obligatory and distinguishing feature of diffuse glomerulonephritis, but is absent in focal glomerulonephritis, in fact in focal nephritis of all types. They believe this invariable hypertension in diffuse glomerulonephritis to be due to the lesions in the glomerular loops, but these are not at all the same as those which they describe as occurring in the arterioles in sclerosis.

They expressly state elsewhere that mere occlusion of vessels, such as occurs in glomeruli, is not a cause of hypertension, and they do not claim that in sclerosis all the vessels are affected before hypertension arises. Sclerosis, in fact, is a typical "focal" lesion, according to their own description, and the surest cause of hypertension, yet when only part of the glomeruli are diseased a diagnostic distinction is absence of hypertension. On the other hand, they do not regard hypertension in glomerulonephritis as regularly dependent on sclerosis, for then they would have to demonstrate or assume the existence of sclerosis in all diffuse, and its absence in all focal glomerular, lesions, which they nowhere attempt.

There are two evident inconsistencies here: (1) considering the changes in the glomerular loops in nephritis equivalent to the arteriole changes in sclerosis, and (2) assuming that hypertension does not result till all the glomerular loops are

involved in nephritis, while it occurs when only part of the arterioles are diseased in sclerosis. It is also weak, it seems to me, to regard a single structure, the glomerulus, as the pivot of renal inflammation, instead of viewing the changes in all the kidney structures more in proportion.

In my opinion Delafield's comprehension of the whole subject is broader, his understanding of congestion, degeneration and acute inflammation clearer and better defined. Chronic nephritis, however, was too difficult for him to solve without the aid of the recent knowledge of renal function. It is to this problem, especially, that Volhard and Fahr address themselves, dividing Delafield's chronic nephritis into nephrosis nephritis, and sclerosis, and in support of their claims they make a most splendid and exhaustive study of renal function and all renal symptoms in the various sub-groups.

The future only can determine just how much of their interpretation will be accorded the value of truth, but whatever the final verdict, their work is full of light and helpfulness to every student of kidney disease.

THE DIAGNOSIS AND TREATMENT OF PYELITIS IN INFANCY AND CHILDHOOD*

ROWLAND G. FREEMAN, M.D.

PYELITIS, so called, is an inflammation of the upper part of the urinary tract, which may or may not be accompanied by an irregular, markedly remitting temperature, and is characterized by a urine with an acid reaction, containing pus and bacteria.

It may sometimes be differentiated from cystitis by the reaction of the urine, the absence of vesicle tenesmus, and very frequent micturition.

That the pus and bacteria in these cases come from the hylus of the kidney, we cannot be sure, but we may assume that they come from either the hylus of the kidney or the ureter.

While some of the cases are acutely sick, most of the cases of pyelitis are found simply by routine examination of the urine. These cases are quite as difficult to cure as cases to which attention is called by acute illness.

DIAGNOSIS

The diagnosis, or the question whether the child has a pyelitis or not, is sometimes difficult to answer. In a male child, in whom this condition is rather rare, the presence of more than one pus cell in a high-power field of a centrifuged urine, usually signifies a real pyelitis. In female children the diagnosis is more difficult, because under ordinary conditions the urine washes the vulva, and pus cells from the vulva or vagina may produce a picture resembling that of pyelitis, although the cells from the vulva wash are not as apt to be in clumps as are those from the upper urinary tract.

This difficulty in diagnosis in a female child stimulated work at The Roosevelt Hospital (which has been reported

* This paper was written especially for The Roosevelt Hospital Report, 1924.

by Dr. Hartshorn) in order to ascertain whether catheterization of the child was necessary either for diagnosis or for determining when the case was cured. This work has shown very definitely that catheterization is not necessary; that in order to obtain a practically uncontaminated specimen the following routine is necessary: The labia of a female child should be separated and the vulva carefully washed with soapy water, rinsed with clear water and dried with a clean towel. The urine should be passed into a vessel that has been rinsed with boiling water, put into sterile bottles with corks that have been sterilized, kept cold until planted and planted as soon as possible. Such urine, when intelligently collected, has a negligible contamination.

Of 94 cases in female children, 48 were sterile as obtained with the catheter, and 42 were sterile as obtained with these precautions. The average contamination as reported by the laboratory was not materially greater in the specimens obtained by sterile precautions than in the catheterized specimens.

If a specimen of urine from a female child, obtained with such precautions, contains several pus cells to each high-power field of a centrifuged specimen, we should be suspicious of pyelitis. An accurate diagnosis can only be made by obtaining more specimens in the same manner and having the urine planted for bacteriological examination. An untreated case of pyelitis contains usually many thousand bacteria to a cubic centimeter, and these bacteria are usually the colon bacilli.

MODE OF INFECTION

The mode of infection in pyelitis has been considerably discussed. The most probable method at first thought would be the external contamination. Babies, in whom this condition is not uncommon, frequently have their movements in the diaper, so that the vulva of the female child would usually harbor the colon bacilli with which the feces abound. The short urethra should give ready access to the bladder, and we know that in the case of the gonococcus an ascending inflammation of the urinary tract certainly takes place. On the other hand, it has probably been fairly

demonstrated that the colon bacilli cannot pass up a normal ureter. Sweet and Stewart cut the ureters in animals and attached their open ends to the lumen of the intestine with no ascending infection. It has, moreover, been shown that bacteria can pass to the kidneys through the lymphatics, and the most direct route is to the right kidney, which is most often affected. Therefore, we must conclude that the greater liability of female children to this disease is due to the lymphatic and blood system.

The tendency of a pyelitis is to continue until it is controlled, although spontaneous cure may take place with improvement in general health. Recurrences have been largely due to the fact that cases have been considered cured when the pus has disappeared, without an attempt to determine whether the bacteria have disappeared. If the latter method were followed far fewer recurrences would be observed.

One should always consider the possibility of a pyelitis being a part of some other general disturbance, such as septicemia or tuberculosis, or having its origin in dental caries or in a bad condition in the tonsils or antra.

TREATMENT

The accepted methods of treatment of this condition are of two sorts. It has been well established that by alkalinization of the urine and keeping it alkaline persistently for several days, a cure can, in most cases, be accomplished. For this purpose bicarbonate of soda, preferably in solution, in doses of from 5 to 20 grains every hour day and night, or every hour during the day with a double dose at bedtime and at 10 P.M. and possibly at 2 A.M., is usually successful.

Another preparation to produce alkalinity, which has been used at The Roosevelt Hospital when bicarbonate of soda alone is not effective, is the administration of calcium carbonate, bicarbonate of soda and burned magnesia, 5 grains each, every two or three hours. There are some cases, however, in which I have found it impossible to alkalinize the urine.

When the alkaline treatment is used, as much aid as possible should be elicited from a proper regulation of the diet, for

it has been shown that a vegetable diet favors an alkaline reaction in the urine. Herbivorous animals have alkaline urine. In addition, certain fruits are effective in this way, such as oranges, raisins, apples and bananas. Tomatoes are not of value, while meats and cereals increase acidity, and plums, prunes and cranberries on account of their content of benzoic acid also increase acidity.[1]

In order to form any intelligent opinion as to what is being accomplished by the treatment it is necessary that there should be in the nursery a supply of litmus paper, and that each passage of urine should be tested with the litmus paper. This paper should be pinned on a sheet stating the time when the urine was passed, such papers being kept in chronological order and brought to the physician with the specimens of urine. In this way only can the physician judge if sufficient alkalinity is being obtained, whether such alkalinity is being kept up day and night, and if not, at what period the child needs greater alkalinity of the urine.

Action of Alkalies. In what manner alkaline treatment cures many of these cases we do not know. Alkaline treatment was first emphasized by Thompson[3] of Edinburgh, a very reliable observer; and Browning[2] states that "the change in reaction bathes the tissues in a more bland fluid and thus enables them to combat the infection more effectually."

Helmholz,[3] who tried experiments to inhibit the growth of bacteria with an alkaline medium, found the greatest alkalinity obtained in urine to be Ph. 8.6, while the colon bacillus is not inhibited by less than 9.2 or 9.6. He also tried the effect on the bacteria of changing rapidly from an acid to an alkali and back to acid, but no difference was observed.

Our results, however, in this treatment are so often quickly satisfactory that we should persist in the alkaline treatment as the most effective and safest treatment we have.

A second method of treatment, often promptly effective when the method just discussed is not, is an effort to sterilize the urine by hexamethylenamin. Occasionally a brilliant result may be promptly obtained with small doses, although Helmholz,[3] in his experimental study, concluded that, on account of the length of time required to produce formalde-

hyde from hexamethylenamin (that is, two hours in order to kill 90 per cent of the bacteria) this has no value in the pelvis of the kidney, as the urine rarely remains in the bladder more than 1½ hours. Thus, even if a sufficient amount of hexamethylenamin is given, it is almost impossible to obtain a bactericidal concentration on account of lack of time.

Again, in this treatment we must not be discouraged by Helmholz's findings, as it does cure the disease. In order to obtain a favorable result, the urine must be acid. The urine, however, is normally acid, and in most cases no aid need be resorted to, excepting avoidance of alkaline medicine, and such modification of diet as is favorable to continued acidity, this diet consisting of the use of cereals, meat, egg, and of fruit only plums, prunes and cranberries.

If under these conditions the urine is not acid, the use of benzoic acid or acid sodium phosphate or dilute hydrochloric acid may be resorted to.

Hexamethylenamin should always be started in very small doses, only ½ grain under one year of age, one grain in children under three and not more than two grains in children from three to five. It may be given in such doses three times a day if well taken, and the dose increased daily until large doses are given, these large doses often curing cases that are not affected by the smaller doses. I have given as much as a drachm a day to children under a year, but only after watching the effect of the smaller doses on such a child for several days. In using the acid treatment the same careful control by litmus papers as used in the alkaline treatment, should be resorted to.

Vaccines. Vaccines are valuable in some cases with fever, if the case does not react readily to treatment. Vaccines, however, do not clear up the urine, but may control the constitutional reaction.

Cases that are not controlled by either the alkaline or the acid treatment, where no complicating conditions are found, may be benefited when specific treatment is stopped and general tonic treatment used. One baby who was made worse by both alkaline treatment and hexamethylenamin, promptly recovered when all treatment was stopped. An older child,

who failed to react favorably to either large doses of alkalies or later to large doses of hexamethylenamin, became entirely well on tonic treatment.

Davis[4] has recently reported cases which he has cured by injections of whole blood.

While I have never used this method for the cure of pyelitis, a case under my supervision with an intestinal infantilism accompanied by a pyelitis, was given a transfusion of 40 c.c. of blood. This transfusion had no effect on the pyelitis, which, however, was finally cured by the administration to this fourteen-months-old child of 15 grains of hexamethylenamin a day.

Cure. When may a case be considered cured? Only when the pus has disappeared from the urine, and when plates made from specimens obtained under sterile precautions are practically sterile.

SUMMARY

The points I have tried to make in this paper are the following:

A diagnosis of pyelitis should always be confirmed by a bacteriological examination of the urine.

Urine may be obtained for such examination by the method here advocated, and catheterization is not necessary.

The treatment should be aided by proper regulation of the diet, and by testing the reaction of all urine passed.

The child should be considered cured only when pus has disappeared from the urine and when a sterile specimen of urine has been obtained.

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BACTERIAL CONTENT OF URINE WITH SPECIAL REFERENCE TO PYELITIS*

W. Morgan Hartshorn, M.D.

IT is the purpose of this paper to discuss briefly the bacterial content of the urine in children, especially with reference to disease, as practically all the work has been done upon specimens obtained from the children's ward of The Roosevelt Hospital.

From another institution urine from twenty-three apparently healthy children was cultured, and a preliminary report of this work will be included.

The literature upon this subject is limited. Ross in 1915 reported upon the examinations of 19 specimens of catheterized urine from apparently healthy children whose ages are not given.

Cultures from 11 specimens were sterile, and 8 showed staphylococcus. Beeler and Helmholz in 1916 reported results obtained in the examination of specimens from 30 girl infants and 31 girls over two years of age.

Their technique: Specimens were obtained by the use of a sterile catheter after a sterile application had been used in the vagina and the parts constantly washed by a 1 per cent lysol solution. One cubic centimeter was planted in litmus lactic agar. Two cubic centimeters were planted in deep dextro blood-agar tubes. In children over two years of age 13 cases out of 31 were sterile. Of 118 specimens examined 61 were sterile, and 57 contained bacteria.

Infants—13 sterile—11 contained bacteria.

Girls over 2 years—38 sterile—22 contained bacteria.

Conclusions: 1. Organisms of the colon bacillus group are not a normal inhabitant of the female urethra.

* This paper was written especially for The Roosevelt Hospital Report, 1924.

2. In extra urinary infections of the first two years the colon bacillus is frequently found in the urethra.

In girls over two years the urine is almost free of organism, entirely free from the bacillus coli group. Helmholz in 1922 reported 70 cases in which the urine was cultured, 35 boys and 30 girls:

All cultures negative in 17 girls and 13 boys.

All cultures positive in 12 girls and 14 boys.

There were 14 instances of staphylococcus, 6 instances of staphylococcus lacteus.

He concludes that the urine is sterile in from one-third to one-half of the cases.

In our series, bacteriological examinations of 23 specimens of urine from apparently healthy children obtained after sterile precautions had been taken (as it was impractical to catheterize), showed, in 11 girls ranging from eight to eleven years of age:

Bacterial growths not exceeding 10 colonies in a plate in 5 cases.
The other plates contained 20–30–40–60–70–100 colonies.

Organisms present—Bacillus Coli Communis	3
Subtilis	3
Proteus	2
Staphylococcus albus	3

In 12 boys ranging in age from nine to fifteen years:

Eight of the twelve plates were sterile.
Four plates contained colonies 7–7–15–15.
The prevailing organism was the staphylococcus albus.

Over one-half of the 23 cases showed sterile specimens.

Passing to the bacteriology of the urine in children suffering from gastrointestinal diseases. Schwartz reports that in the examination of specimens from 63 infants, from 38 to 60.3 per cent showed a gram-negative organism. He concludes that actual bacilluria is twice as prevalent in girls as in boys.

At the request of Dr. Freeman a bacteriological study of the urine of patients in the Bliss Ward of The Roosevelt Hospital was made to determine:

(*a*) The growth in a culture of urine from children suffering from various diseases, compared with those suffering from pyelitis.

(*b*) The comparative growth in culture from specimens of urine obtained in different ways.

When it was possible, 3 different specimens of urine obtained from a patient the same day were examined. These specimens were designated.

1. Routine. This was the ordinary morning specimen of urine sent to the laboratory in a sterile bottle.

2. Sterile. This specimen was obtained after the external genital of the child had been cleaned with soap and water and washed with sterile water, and the specimen passed into a sterile receptacle and sent directly to the laboratory.

3. Catheterized. Obtained with the usual aseptic precautions. Technique: Two-tenths of a cubic centimeter from each of the different specimens was planted in agar and the plates then incubated for twenty-four hours. The colonies upon the different plates were then counted.

Series of these plates were made from 127 cases. Thirty of these were discarded, as they were obviously contaminated. The remaining 90 cases are divided as follows:

18 Cardiacs
26 Pyelitis
11 Bronchitis
11 Pneumonia
31 Miscellaneous

This last group included chorea, lung abscess, anemia, encephalitis, tonsillitis, rheumatism, pleurisy, tuberculosis, convulsions and Hodgkin's disease.

The average number of colonies in each group was:

	Routine	Designated sterile	Catheter
18 Cardiacs	3272	16 (16)	12 (10)
26 Pyelitis	3413	430 (26)	49 (20)
11 Bronchitis	3679	59 (11)	2 (10)
11 Pneumonia	1828	31 (11)	18 (8)
31 Miscellaneous	1704	196 (31)	5 (18)

Numbers in parentheses indicate the number of cases.

Plates with no growth were obtained in 38 of the designated sterile and in 45 of the catheterized specimens out of 83 cases in which both specimens were obtained.

Cardiacs.	10 out of 16 designated sterile specimens—62.5 per cent
	7 out of 10 cath.—70 per cent
Pyelitis. .	10 out of 25 des. s. specimens—40 per cent
	8 out of 19 cath.—42 per cent
Pneumonia.	0 out of 11 des. s. specimens—81 per cent
	7 out of 8 cath.—87 per cent
Bronchitis. . .	8 out of 12 des. s. specimens—66.6 per cent
	9 out of 10 cath.—90 per cent
Miscellaneous	15 out of 31 des. s. specimens—48 per cent
	14 out of 19 cath.—74 per cent

Of the original 127 cases 115 were females, 12 males. All the catheterized specimens were from females. Their ages ranged from three to eight years. All the pyelitis cases were infections from the coli communis bacillus. A few infections from staphylococcus and proteus were found among the others.

The pyelitis cases demonstrated that while the clinical symptoms and the examination for pus might be negative, yet cultures from the urine might show an extensive growth of colon bacilli.

The following conclusions are to emphasized:

1. In healthy children the urine is free from bacteria in at least one-half the cases.

2. Cultural growth in specimens obtained with sterile precautions is very slightly in access of that obtained by catheterization.

3. For bacteriological examination of the urine catheterized specimens are desirable, but not essential, for practical purposes.

4. Children suffering from pyelitis should not be discharged as cured until cultured specimens of their urine are free from bacteria.

5. The urine obtained by sterile precautions or by catheter contained a far greater number of bacteria in pyelitis than in any other disease studied.

I wish to express my thanks to Dr. Lyle, director of the Roosevelt laboratory, to Dr. Sanford, bacteriologist, and to

Miss Fletcher, technician, for the bacteriological work in connection with this paper.

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RECOVERY AFTER POSTOPERATIVE TETANY TREATED WITH CALCIUM LACTATE *

WILLIAM P. HEALY, M.D.

FROM time to time the occurrence of tetany has been noted following various operative procedures, more especially the removal of the thyroid or parathyroid glands, or operations upon the abdominal or pelvic viscera. The prognosis, as a rule, in postoperative tetany has been bad. In recent years a great deal of experimental work has been done, more especially on parathyroidectomized dogs, and careful studies of the blood-chemistry changes in these animals made before, during and after attacks of tetany.

Probably the most important of the earlier studies were those of MacCallum and Voegtlin. These investigators in 1908 noted that after parathyroidectomy the calcium concentration in the blood and tissues was less, and in the feces and urine was greater, than normal.

MacCallum and Vogel in 1913 confirmed the above findings and reported an average of 2.7 mg. of calcium per 100 gm. of the whole blood in tetany as against 6.1 mg. in normal dogs. Briefly then, tetany in these animals was assumed to be a result of calcium deficiency, and more especially so since the administration of calcium salts was found to be most effective in relieving the symptoms.

More recently Hastings and Murray, in a careful series of experiments on dogs, have confirmed the above findings. They showed that the concentration of calcium in the blood decreases rapidly, beginning soon after removal of the parathyroids, and they were able to demonstrate repeatedly the temporary curative power of intravenous calcium chloride injections for tetany.

During the last few years cases of tetany have been reported following the intravenous injection of sodium bicarbonate for therapeutic purposes.

* Reprinted from *J. Biol. Chem.*, March, 1921, and *Am. J. Obst. & Gynec.*, Jan., 1922.

Recently, the writer* reported a series of 6 cases of postoperative tetany, 4 of which resulted fatally, due to the administration of large quantities of sodium bicarbonate per rectum. Those cases received approximately 2400 grains sodium bicarbonate per rectum within six hours after operation; and despite the fact that some of it was expelled, enough was retained to bring about the symptoms of tetany.

The following case is reported because a much smaller quantity of bicarbonate of soda was administered (about 600 grains):

Female, aged thirty-two, married seven years, no children, family and personal history excellent. Menstrual history normal except for severe dysmenorrhea on first and second days. Chief complaints: Sterility, dysmenorrhea, severe backache, occasional attacks of dysuria. The patient was a well-developed, healthy-looking woman and the physical examination was negative except for the pelvis. The cervix was lacerated (postoperative) and the uterus was enlarged to the size of a grapefruit by two fibroids.

Operation. Nitrous oxide and ether anesthesia. Duration 1 hr. 15 min.; dilatation of cervix, tracheloplasty, multiple myomectomy and hysteropexy. There was a moderate amount of bleeding during the myomectomy, but the patient was returned to bed in excellent condition with a pulse of 100, temperature 98.80, respirations 22, at 10.10 A.M. At 10.45 morphine sulphate $^1/_6$ grain (hypo); at 11.45 rectal enema containing 192 grains glucose, 300 grains sodium bicarbonate, 40 grains sodium bromide and 8 oz. tap water at a temperature of 106° was given and retained; and at 3.15 P.M. the enema was repeated without the sodium bromide. At 6.00 P.M., temperature 103.4°, pulse 130, respirations 10.

The patient was conscious, but her respirations were very shallow and slow, the pupils were not contracted and responded to light. She was given atropin sulphate $^1/_{150}$ grain (hypo) about 7.00 P.M. She voided $5^1/_2$ oz. urine, the pulse and temperature continued to rise and at 8 P.M. temperature was 104.8°, pulse 130, respirations 10.

Despite the high temperature, rapid pulse and slow respirations the patient did not complain. She was fully conscious

*Am. J. Obst. & Gynec., Aug., 1921.

and mentally quiet but rather restlessly moved her arms and legs about.

She received no further sedative and went through the night fairly well with a little disturbance from nausea until 6.45 A.M. when she suddenly complained of stiffness of her hands and a numbness and tingling of the entire body and difficulty in breathing.

The examination showed the typical bilateral tonic spasm of tetany involving both hands with also slight flexion of wrists and elbows. Associated with this, about every three minutes a wave of numbness would sweep over the body accompanied by rapid breathing and intense spasm of gastric and abdominal muscles with vomiting of an ounce or so of clear fluid.

The anxiety of the patient was extreme and her requests for relief were insistent.

Calcium lactate, 20 grains, with $\frac{1}{2}$ oz. lime water was given by mouth every half hour for six doses, beginning at 7.30 A.M., and the greater part seemed to be retained. By 11 A.M., the spasm of the hands was much less marked, but the tachycardia and attacks of numbness and rapid breathing still continued, and at 11.35 an intravenous injection of 100 c.c. water with 1 gm. of calcium lactate was given. The result was most striking. Before the injection was finished the tachycardia and all the other symptoms disappeared and the patient became most comfortable. Thereafter the convalescence was normal.

It would seem that the symptoms of this case can be explained by a more rapid absorption of sodium bicarbonate into the blood stream than the kidneys were able to take care of by elimination, because of a temporary depression from the operative procedure, and this brought about a disturbance of salt metabolism, especially in the balance between sodium and calcium.

This balance was restored by the administration of calcium salts and the symptoms disappeared.

REPORT OF A CASE OF INTRACTABLE VULVAR ULCER (ESTHIOMENE) CURED BY PROTEUS VACCINES*

WILLIAM P. HEALY, M.D.

THE term esthiomene is derived from the Greek word meaning to eat or corrode. In 1849, it was applied, in a thesis by P. C. Huguier, particularly to a gnawing or corroding eruption of the vulvoanal region. He divided the cases into three clinical types, any one of which might occur alone or in combination with the others. In the first group the lesions were superficial, ambulant, serpiginous, ulcerating, healing in one place and progressing to ulceration in another place. In the second group the lesions were deeper and more destructive, perforating the tissues. In the third group the destructive features were overbalanced or replaced by edematous infiltration, hypertrophy, or even a condition resembling elephantiasis.

The disease occurs as a rule in adults, is chronic and exceedingly resistant to treatment, at times seeming to be cured but soon reappearing and progressing more rapidly. The origin of the disease is obscure, and although usually regarded as due to venereal infection, has not yielded to treatment along these lines.

The patients have usually died from exhaustion or intercurrent infections.

The subjective symptoms are an intense burning sensation and extreme constant pain in the lesions, requiring the use of morphine for relief.

The following case which would seem to belong in Group 1 of Huguier's classification, came under my observation in September, 1919:

Female, age twenty-two, married eight months.

The patient's mother died at forty-one years of cancer of the left cheek; otherwise the family history is entirely negative for cancer, tuberculosis or

* Read at a meeting of the New York Obstetrical Society, May 9, 1922. Reprinted from *Am. J. Obst. & Gynec.*, Sept., 1922.

syphilis. The woman's general health was always excellent until the onset of present illness. Her menstruation was normal except for severe backache during the period. At time of admission, patient was about six months pregnant. Her chief complaint was due to ulcer of the vulva, giving intense pain. The present illness began in 1915 with the development of a small blister, the size of a pinhead, on the left labium majus, which caused a burning sensation and two days after its appearance broke open and discharged a small amount of serum. It then began to pain a great deal, especially when irritated by urine, and a physician was consulted. He made an examination of the blood and urine, which were negative, and treated the lesion with iodine and salves. It soon healed and remained so for nearly six months, which was the longest period of quiescence since the onset. It then broke down again and under similar local treatment was soon healed, but thereafter would reappear at intervals of from one week to a month, slowly healing under local treatment and not always reappearing in the same place.

The patient married in December, 1918, and thereafter, as a result of irritation from intercourse and the urine, the ulcer rarely healed for more than a few days at a time. During the first few months of her marriage, the patient was anesthetized on four different occasions, and the ulcers were cauterized without success. Silver nitrate applications distinctly aggravated the lesion and added to the patient's distress. The chief symptom throughout has been intense pain and burning in the ulcers and the adjacent tissues.

In August, 1919, despite a negative blood Wassermann test, a clinical diagnosis of syphilis was made, and the patient was given six intravenous injections of a French salvarsan solution without influencing the lesion.

The patient conceived two months after her marriage and there seemed to be no doubt that the congestion of the tissues of the vulva, as a result of pregnancy, was a factor in increasing the spread of the disease. A local examination of the patient at this time (Sept., 1919) showed a marked lividity of the tissues of the vulva with a very moderate induration and edema of the subcutaneous structures. At about the middle of the left labium majus there was a deep transverse scar, due to the cauterization. The right labium majus and adjoining surface of the thigh were covered by several irregular, superficial ulcers, which tended to coalesce and extend down the inner side of the right buttock toward the anus. The edges of the ulcers were slightly undermined in places and were not especially firm, the base was yellowish and bled easily, and the raw surfaces were exceedingly sensitive to the slightest touch.

The plan of treatment followed at first was extreme cleanliness and constant protection of the lesion from external irritation, and for a few days the lesion seemed to heal along the upper margins, but continued to spread below. The patient was then taken to the operating room and the lesion excised, and the raw surface thoroughly cauterized. This was done on October 10, 1919. A microscopic report on this tissue was: "Infected skin ulcer with necrosis." There was no improvement in the patient's condition following this treatment and thereafter for a period of one month the local treatment was carried out by means of wet dressings of various solutions, such as boracic acid, soda bicarbonate, tincture of myrrh, hydrogen peroxide, Dakin's solution, neosalvarsan locally, and ointments of various kinds, without avail. The condition of the

patient was pitiable and precarious, and the pain of the lesion was constant and most intense. She was receiving a grain or more of morphine sulphate daily, hypodermatically, and 5 per cent cocaine ointment was being applied to the ulcers. The lesion gradually spread, involving the lower portion of the vagina

Fig. 36.

and nymphae, causing a slough of the perineum, extending across to the left buttock and around the left side of the anus. It was feared that the fetus would succumb to the morphine and codeine, and as even a dead fetus could be delivered only with difficulty and considerable risk to the mother through a

diseased vulva, it was decided to do a cesarean section, Nov. 7, 1919, four weeks before term, in the hope of saving the baby, which seemed to be well developed at that time. This operation was done on that date, and a male child weighing 6 lbs. and ½ oz. was extracted.

The baby breathed spontaneously and seemed to be in every respect a normal infant, free from any evidence of congenital syphilis. The patient's convalescence was normal despite an infected abdominal incision. The ulcers seemed to improve during the puerperium. During this time two *x*-ray treatments a week were given with the hope of stimulating the tissues to heal. After a preliminary improvement, however, it was evident that no definite headway was being made and that the patient was really gradually losing ground.

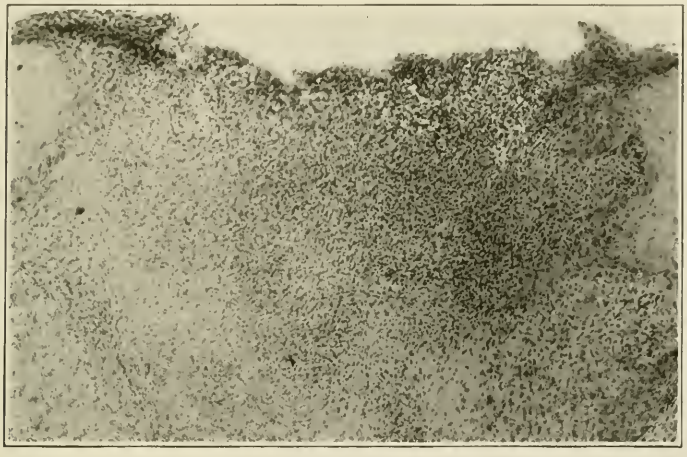

FIG. 37.

In January, 1920, a transfusion of 500 c.c. of blood was given and a day or two later the entire ulcerating area was completely excised and the raw surfaces closed with silkworm gut sutures. The result was apparently very successful, and the lesion appeared, for a short time, to be cured. It soon recurred, however, and spread rapidly, and in March, 1920, another excision, more extensive than the preceding, was carried out, and a plastic operation to cover in the raw areas was done at the same time. This operation also appeared to be a success, the entire surface area being healed. In June, 1920, however, immediately in the center of the transplanted area, there was a small recurrence. This was promptly excised. Late in July the lesion broke out again.

The pathologist's report on the tissues removed follows:

"Specimen consists of excised vulvar ulcers and the subcutaneous tissues surrounding them. There is some ingrowth of epithelium into the bed of the ulcer, which is grayish red, and somewhat necrotic. The edges of the ulcers are not undermined and the surface epithelium grows down into the bed of the

ulcer. Sections were taken from various portions of the ulcers, and all seemed to show the same pathological condition.

"The stratified squamous epithelium of the skin, where it is intact, appears normal, containing both hair follicles and sebaceous glands. Following the surface of the skin area one suddenly comes upon an area of ulceration where the entire dermis is destroyed. This is a healing ulcer as the floor is made up to quite a depth of well-organized tissue, with cellular infiltration and proliferation of the blood spaces. The depth to which the ulceration has extended, as indicated by the lowest point at which the granulation tissue begins, is on the superficial perineal muscles. These muscles and the fatty and connective tissues around them are infiltrated especially around the blood spaces, with foci of small round cells and polymorphs. There is no extensive necrosis in the lesion at present. Sections stained with methylene blue have been made in an attempt to bring out the nature of the bacteria within the ulceration. Only cocci are seen and these are probably staphylococci and streptococci of secondary infection. No specific organism has been found by the staining methods employed. The epithelium of the ulcer edge shows only a slight tendency toward proliferation and ingrowth.

"The failure of the epithelium to grow over the granulation tissue cannot be due to the poor blood supply, as these sections show the presence of numerous blood spaces. However, as a theoretical cause for the lack of healing power in the tissues one might suppose that a specific organism—if it is such —that causes such a deep and widespread ulceration and loss of tissue, may well be able, when still present in the tissues, to destroy the new tissue as it is formed, or at least to retard its normal repair; and that the granulation tissue having more resistance than the new growth of epithelium, proceeds at a more rapid pace, while the epithelial edge seems to be almost at a standstill."

Just after the operation, while the excised tissue was still sterile, cultures were made aerobically and anaerobically by placing pieces of tissue in the media. A short chain nonhemolytic streptococcus was grown in both the aerobic and anaerobic media. These were obtained in pure culture. A dilution of 1 to 100 was made in normal saline and 0.5 c.c. of this solution injected into the skin of a guinea pig and 0.2 c.c into the skin of a mouse. Both animals were alive and well without any appearance of a lesion at the site of injection, a week later. Then a dilution of 1 to 10 was made from the pure culture and 1 c.c. of this solution was injected into the skin of a guinea pig and 0.5 c.c. into the skin of a mouse. The mouse died twenty-four hours and the guinea pig seventy-two hours, after the injection. Autopsy revealed nothing in either case at the site of the injection or in other organs. The culture died out before further injections were made. The opinion of the bacteriologist is that these organisms are not in any way the specific cause of the lesion, but simply secondary contamination of the ulcerated areas.

In September, 1920, smears and cultures were made from the surfaces of the ulcer, by Dr. Thomas S. Winslow. Practically a pure culture of proteus was obtained, and as this was not regarded as of any importance, the cultures were repeated, and again the proteus was the predominating organism. At the suggestion of Dr. Winslow a proteus vaccine was made and on Oct. 1st the administration of this vaccine was begun, and was kept up at intervals of three to

four days, starting with a dose of 50,000,000 and increasing until the patient was receiving 500,000,000 at each dose. This treatment was continued without interruption for three months until the patient had received 30 doses of the vaccine.

Within ten days after the beginning of the treatment the pain left the ulcers and they began to heal. In one month they had completely disappeared. The improvement in the patient's general health was also remarkable, with the disappearance of the local lesion and the cessation in the administration of codeine and the use of cocaine ointments. The lesion remained healed from November, 1920, until about May 1, 1921, when there was a recurrence. Cultures were promptly made from the lesion by Dr. Winslow, who again obtained the proteus but in combination with a bacillus lactis aerogenes and a fungus.

A vaccine of the proteus was made and again administered and the lesion which was showing a tendency to spread, rapidly and promptly responded to the administration of the vaccine, and in six weeks had entirely disappeared. The patient has, up to the present time, remained free from any recurrence.

The manner of development of the lesion was always the same—the patient would experience a burning sensation in an area of the vulva and within twenty-four hours a minute herpetic vesicle would appear at this point, gradually enlarging to about 1/16 or 1/8 in. in diameter, and would then break down, leaving a small raw surface. The lesion all the time resembled a simple herpes. After the appearance of the ulceration the pain would become much more severe, and the patient would show distinct constitutional depression at this time. The ulcer would then gradually enlarge, and the epithelial tissue appear to dissolve and melt away slowly—the lesion growing always superficially and in a serpiginous manner. After a time there would be a tendency to healing in some areas, but this was never complete.

The proteus, in pure culture or in association with other organisms in pathologic conditions has been isolated from time to time by various investigators since 1889. While this organism is ordinarily regarded as nonpathogenic there is ample evidence, according to Wenner and Rettger, to show that it may assume a pathogenic rôle, and thus occupy a position analogous to the pyogenic micrococci.

CONCLUSION

There would seem to be no doubt that this case corresponds to the lesion first described by Huguier in 1849. There would also seem to be no doubt that in this instance the persistence of the lesion was due to the presence of the proteus bacillus, which through its toxines or in some other manner brought about a solution and destruction of the tis-

sues, which persisted despite all local medical and surgical measures until the proteus vaccine was administered. This brought about prompt relief from pain and the rapid healing of the raw surfaces.

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FUNCTIONAL TESTS OF THE CIRCULATION AND THEIR SIGNIFICANCE*

W. W. Herrick, M.D.

INTRODUCTION

THE practitioner of today is, for better or for worse, tending to stray from the morphological or structural point of view in medicine. His search is becoming less for changes in form, more for changes in function. Not so much is he concerned with how an organ looks or feels or sounds, as with what it will do: not appearance, but performance.

In cardiology, we have been long in passing through the era begun by Laënnec and his stethoscope. For quite a century, meticulous descriptions of physical signs held the field. Vital decisions were based on the presence or absence of murmurs or enlargements. This era was supplemented by a period characterized by the application of instruments of precision—the sphygmograph, sphygmomanometer, the polygraph, electrocardiograph and electrophonograph—to the study of the heart. This period seems now to be merging with one in which study of the functional response is paramount. In view of this trend, we may, therefore, profitably inquire into the development and practical value of the various means proposed for the estimation of circulatory function or efficiency.

THE EARLIER TESTS OF MYOCARDIAL EFFICIENCY

These methods began to appear in the medical literature about 1905. One of the earliest is Herz's[1] "Selbstemmungsprobe." This is performed by carefully noting the pulse rate at rest, then slowly flexing the forearms while opposing the movement forcibly by bringing into play the extensors. Herz believed that such exercise of strain in normal individ-

* Read at the Annual Meeting of the Medical Society of the State of New York, Albany, N. Y., Apr. 19, 1922. Reprinted from *N. York State J. Med.*, Feb., 1923.

uals causes no change in pulse rate, while in those with feeble hearts, the pulse rate is slowed five to twenty beats per minute. American observers, Cabot and Bruce,[2] also Hirschfelder,[3] while subscribing to Herz's findings in the main, note sufficient exceptions so that the method seems to them, in general, unreliable. Apparently, Herz's test has not survived criticism and has only historic value.

One of the earliest functional tests is a development of Marey's[4] studies (1881) in which he showed that in normal individuals with simultaneous compression of both brachials and femorals, the blood pressure rises. Katzenstein[5] showed that in individuals with decompensated hearts subjected to similar arterial constriction, the blood pressure is unchanged or falls. Subsequent observers (Hoke and Mende)[6] have corroborated these results in general, but consider the test unreliable and too dangerous and painful for general use. This test, with its numerous modifications, has also passed into disuse.

GRAÜPNER'S TEST

In 1905, Graüpner[7] published his studies on the rise of blood pressure following exercise. He found that moderate effort, such as rapid walking, was followed by a rise of blood pressure in normal persons while those with failing hearts showed a fall. These observations were confirmed by the careful work of Baur,[8] and in the United States, by Cabot and Bruce.[2]

In 1906, Graüpner[9] published the most comprehensive of his studies on the rise of blood pressure following exercise. His conclusions were:

1. A moderate amount of work in well-trained individuals causes no change in systolic blood pressure.

2. An increase in work causes an immediate rise in systolic blood pressure, and this returns promptly to normal.

3. If the work is increased to the point of strain, there is, immediately after work, a fall in blood pressure followed quickly by a rise to a point above the normal, and a later return to normal. Graüpner regarded this primary fall in blood pressure and secondary rise above normal as indicating "functional insufficiency of the heart."

Barringer,[10] taking Graüpner's basic idea, made further clinical studies of the effect of exercise upon blood pressure. This work is, in summary, as follows:

Barringer studied the effect of carefully measured amounts of work upon the systolic blood pressure. He concludes that (1) a delayed rise in systolic pressure after work in a normal person, or in one with cardiac insufficiency, indicates that the preceding work had either made the heart temporarily insufficient or had increased an already existing insufficiency. (2) "If the systolic blood pressure reaches its greatest height not immediately after work but from thirty to one hundred and twenty seconds later, and if the pressure immediately after is less than the original level, that work has overtaxed the heart's functional capacity and may be taken as an accurate measure of the heart's efficiency." Using this standard, Barringer found that a cardiac capacity under 1000 foot-pounds per minute affords important confirmatory evidence of myocardial disease. Mann[11] found that, in a small group of convalescents, there was a progressive increase in the amount of work necessary to produce this "delayed rise" of blood pressure as clinical improvement took place. In a study of the circulatory reactions to graduated exercise in normal children, Wilson[12] finds this test of value.

In most other quarters, however, one meets dissentient views. From the clinician's viewpoint, a serious criticism is that Barringer took account of rises in blood pressure frequently as small as 4 mm. Hg. So commonly does the systolic blood pressure vary 5 to 10 mm. or more within a few seconds and under such a variety of conditions that most observers will agree that variations under 6 or 8 mm. are often within the limits of error or of physiological variations and cannot form a solid basis for important conclusions. Again, Rapport,[13] in a careful study of the response of the blood pressure to exercise, finds that the time intervals are all-important. He states that, provided there is any reaction to exercise, rise is always present, whatever the amount of work. With increasing amounts of work, the rise is prolonged. The summit of the blood-pressure response to different amounts of work is reached within twenty to sixty seconds and is not prolonged beyond sixty seconds. The curves reach a normal level in times varying

with the amount of work—from one to four minutes. In cases of moderate exercise, the rise in blood pressure is completed promptly—too promptly to afford time for reading except by the use of special methods. In more prolonged effort, the reading may be taken on the rise since the rise is delayed. To speak of this delayed rise as an index of circulatory efficiency is, in Rapport's opinion, unsound and, at best, an assumption. On the clinical side, Mabon,[14] in a study of effort syndrome with measured work, found that when such cases were exercised even to the limit of their strength a delayed rise of blood pressure was observed so "rarely and inconstantly" that it had no value in estimating the circulatory capacity of this group of cases. In a personal communication, Dr. Burton-Opitz gave the opinion that a delayed rise in blood pressure after effort is too inconstant and unreliable to have any practical value as a measure of cardiac reserve force. From the standpoint of physiology and of clinical observation it would, therefore, seem precarious to base sweeping and positive deductions respecting the efficiency of the myocardium upon the behavior of a single circulatory factor with its complex of relationships which might modify its response and adjustment to varying conditions.

Whatever the merits of the bygone controversy, the test has been superseded by methods grounded upon simpler and more generally accepted physiologic facts.

THE BLOOD PTOSIS TEST (CRAMPTON)

From this point in the evolution of tests of circulatory efficiency, we proceed from the simple to the elaborate. Crampton[15] leads with his work on "blood ptosis" or "the gravity resisting ability of the circulation." This is not offered by its originator as a test of myocardial function, but rather as an indication of the efficiency of the influences which bring the blood to the heart when the body is in the upright position, and through them a measure of the efficiency of the individual. In this test, there are two factors: the pulse rate and the systolic pressure, each of which may vary in either direction when the subject changes posture from the horizontal to the vertical—the increase in systolic pressure tending to indicate efficiency, and an increase in heart rate the reverse.

The test is performed as follows: The patient lies down until the pulse becomes stabilized. The systolic pressure is then recorded. The patient then stands until the pulse rate reaches a "standing normal" or stabilization, when the systolic pressure is again measured. The resulting increase or decrease in systolic pressure and in pulse rate is used in conjunction with a standard table to find the individual's index. In health, the index varies from 50 to 100. While a "low gravity resisting power" on the part of the circulation is evidenced by a low index, some diseased conditions show very high indices. Crampton, himself, frankly says that the test is extremely rough and may be misleading. The work is, however, of importance intrinsically and as a development; it seems based on sound physiology and, if not trusted too far, is helpful clinically. It is of special use in indicating a change in an individual's general condition. As Crampton remarks, "a decline in the blood ptosis index may precede any other evidence of the onset of an acute disease."

Sewall[16] has extended somewhat the clinical study of the postural changes in blood pressure. He emphasizes the significance of the rise in diastolic pressure on assuming the erect posture after lying down, as an important contributory evidence of poor adjustment to gravity on the part of the circulation. The rise in diastolic pressure may take place with or without a coincident fall in systolic pressure, the end effect being a fall in pulse pressure. This fall in pulse pressure in turn denotes a lessened stroke volume of blood to meet the demand caused by the effort to assume and maintain the body erect, and is a fairly dependable criterion of the general physical efficiency of the individual. In the opinion of Sewall, "excessive fall of systolic pressure in the erect posture indicates weakness of vasomotor control. Excessive rise of diastolic pressure denotes vascular spasm and abnormal effort." Sewall finds that the usual cause of lowered pulse pressure in the erect posture is a rise of diastolic pressure. This he believes indicates lack of contractile vigor on the part of the ventricles, which may be helped by small doses of digitalis.

SCHNEIDER'S SYSTEM OF RATING

Although brought forward as a means of measuring the general capacity or fitness of the body as a whole, Schneider's[17] system of rating is a development of importance in the estimation of circulatory efficiency. This rating is arrived at by combining the results of the blood ptosis and the simple exercise tests. In arriving at a rating, Schneider uses six factors:

1. The reclining pulse rate.
2. The standing pulse rate.
3. The pulse rate increase on standing.
4. The increase in the pulse rate after exercise.
5. The time required for the pulse rate to return to normal after exercise.
6. The difference between the systolic pressure in the reclining and the standing postures.

A point system is suggested for convenience in reading the cardiovascular rating. The scores for each of the six items range from plus 3 to minus 3. A perfect score—plus 3—for each of the six items would be 18. For details, the reader is referred to Schneider's[17] original paper and the accompanying table taken from this paper. Schneider found that a score of 9 or under gave indication of physical unfitness.

Scott,[18] in the exacting demands of the aviation service, found Schneider's the only efficiency test giving reliable information as to the fitness of men for flying. He found that Crampton's test gave no sharp line of demarcation between the fit and the unfit. With Schneider's rating, when a man was found with a score of 7 or less, he was usually unfit for aviation, while those with a score of 8 or more were generally fit. Scott found that loss of sleep, infections, excesses and fatigue had prompt effect in lowering the ratings.

Schneider's ratings are apparently based on sound physiology. In his paper, he quotes the interesting comparison of Dreyer in the case of the rabbit and the hare, which brings out some fundamental facts in the consideration of circulatory efficiency. The rabbit depends upon the burrow for safety and leads a relatively sedentary life, while the hare dwells in the open, his sole means of defense his speed.

Specimens of equal weight show the following contrasts: The hare has double the blood volume of the rabbit, 30 per cent more hemoglobin, and three times more heart muscle. The respiratory rate of the hare is 18 to 20; of the rabbit, 50 per minute. The pulse rate of the hare is about 68; that of the rabbit, about 200. No dissimilar comparison can be drawn between the trained athlete and the flabby sedentary worker. A slow pulse rate and a slow respiratory rate characterize the man in training and he responds to effort with much less acceleration of pulse or respiratory rate than does the untrained individual. Again, as Crampton has observed, the gravity-resisting capacity of the circulation in the trained individual is greater than that of the untrained.

RESPIRATORY FACTORS

The tests thus far mentioned have invoked only circulatory factors. Can any others be brought into the equation of circulatory efficiency? With the further development of the subject, this is possible. Certain respiratory factors are worthy of consideration. The simplest may be termed the "Breath holding test." In normal individuals, the ratio of time in seconds during which the breath can be held may be expressed as follows: 40 to 70 on inspiration, 20 to 35 on expiration. In cardiac insufficiency, the ratio is preserved, but the figures are smaller—averaging 25 to 15.[19] This ability to hold the breath probably varies with the vital capacity. The vital capacity—the volume of the greatest possible expiration after the greatest possible inspiration—has been particularly studied by Peabody.[20] This observer states that the average volume of an ordinary or normal respiration is about 10 per cent of the vital capacity. He gives as an average vital capacity for normal males, 4,000 to 5,000 c.c.; for females, 3,000 to 4,000 c.c. He found a close relationship between dyspnea and decline in vital capacity. In patients with 90 per cent or more of the normal vital capacity, there were no cardiac symptoms; in those with a vital capacity of 70 to 90 per cent, there were exertional dyspnea and a lessened cardiac reserve; among those with a vital capacity of 40 to 70 per cent of the normal, all could walk, but only 7 per cent

worked; those with a vital capacity of less than 40 to 45 per cent were in bed. This observation is a corollary to the earlier observations of Peabody[21] that patients with cardiac disturbance are unable to meet the demands for added pulmonary ventilation as are normal subjects. There is a "limitation of the depth of breathing" which is a large factor in cardiac dyspnea.

Another interesting sidelight with some practical bearing is Peabody's observation that in cardiac patients presenting a lowered vital capacity the basal metabolism was raised 12.8 per cent, while those with a vital capacity of 60 per cent or more gave a figure of 2.5 per cent above normal. This supplements the finding of Peabody, Meyer and DuBois[22] that 9 of 12 cardiac patients with dyspnea showed an increased oxygen consumption from 25 to 50 per cent above the average normal. In the same paper is brought out the fact of an increased minute volume of air in those having the lower vital capacity. The bearing of this on exertional dyspnea is obviously direct. Its cause is found in the probable decrease in the respiratory surface and a relative increase in the dead space in the patient with severe heart disease. This, in turn, has bearing upon the greater proportion of oxygen and the lesser proportion of carbon dioxide found in the alveolar air of such patients as compared with normal individuals.

At this point, the work of Peters and Barr[23] may be mentioned. They observe that in health the difference between the carbon dioxide content of arterial and venous blood is not large and is comparatively constant. In conditions of impairment of the efficiency of the general circulation or of ventilation of blood in the lungs, a disturbance of the ratios is to be looked for. They further note that the "patient with cardiac decompensation maintains his alveolar carbon dioxide at a lower level than does the normal individual, and the level to which he will permit it to rise under the influence of rebreathing is proportionately reduced." These observers state that the increase in the minute volume of effective or exchange air is not explained by the higher level of metabolism, but is necessitated by the low concentration of carbon dioxide in the exchange air. Any great increase

in ventilation is impossible "because of the diminished effective lung volume of decompensated cardiacs."

The complexity of the problem involved in any method attempting to estimate circulatory efficiency from every aspect finds further illustration in the work of Pearce.[21] This student insists upon the interdependence of the metabolic rate in the tissues, the pulmonary ventilation and the capacity of the heart to deliver blood. He states that so long as the demands of the tissues for oxygen and for the removal of waste products are met by adequate and coordinate functioning of circulation, of the processes of gas exchange in the lungs, and of internal or tissue respiration, the mechanism of the body is in equilibrium, which means comfort and efficiency. However, let any member of this vital triad fail to keep pace with the others, there is at once discomfort and inefficiency.

As Pearce adds, it is important in the study of myocardial function to appreciate that the limitations in the vital triad of heart, lungs and internal or tissue respiration usually lie in the heart muscle. In other words, breathlessness on effort is due to inability of the heart to furnish sufficient blood flow to supply the needs of the tissue for the added oxygen called for by the effort. The normal lung, with its factor of safety of 1000 per cent, can probably always keep pace with the gaseous demands of the tissues. The tissues can probably utilize a sufficient amount of oxygen to meet all demands. The limitation is in the capacity of the heart to deliver sufficient blood to meet the metabolic demands of the tissues. It is clear, therefore, that a measure of functional capacity of this basic triune mechanism must, under ordinary conditions, be a measure of the capacity of the heart.

Pearce suggests that the measure of the pressure gradient of carbon dioxide in the blood passing through the lungs—the difference in carbon dioxide tension between the afferent and the efferent blood as regards the lungs—is a reasonably accurate though indirect measure of cardiac efficiency. This test is too technical and difficult for ordinary clinical purposes, but it is useful as a development. It shows the increasing recognition of extracardial factors in all efficiency tests. While this study of Pearce's might, at first, appear

to the clinician to complicate the study of cardiac efficiency, it in reality simplifies it through its emphasis upon the relative weakness of the myocardium in the trinity of vital functions and the fixation of responsibility upon the heart in the event of lack of proder response of the body to stress.

In summarizing the clinical worth of the efficiency tests involving respiratory factors, it may be said that, with the exception of that for the vital capacity, they have more academic than utilitarian interest. Thus far they do not serve the physician where he most needs help—in the detection of slight or early variations from the normal. Among them, the test for vital capacity alone meets this demand and is of unquestioned value.

THE ELECTROCARDIOGRAM

The electrocardiogram has added much of interest to the study of the heart, but it has to most of us been somewhat disappointing in the extent of its clinical aid. The electrocardiogram records not the force or contractile power of the heart, but the point of origin, course, velocity and voltage of the excitation wave as it passes through the heart muscle. By its aid we get evidence of the rate, rhythm, location of the pacemaker, path, direction and velocity of the excitation wave, and representation of disproportion of muscle mass of different parts. Evidence as to the character of the heart muscle derivable from it must be indirect, limited, and subject to variable interpretation. Not infrequently, for example, a diseased heart gives a normal electrocardiogram. However, when recognized changes occur in the electrocardiogram, and are confirmatory of symptoms or physical signs—or both—the clinician can offer an opinion with added assurance.

Such electrocardiographic evidence as may be of value in estimating the character of the myocardium may be summed up as follows: Evidence of auricular damage, such as changes in the P wave, the oscillations of fibrillation and flutter; evidence of damage to the His' bundle, such as a prolonged or irregular P-R interval; evidence of damage to the pacemaker, such as nodal rhythm, extrasystoles, and other variations in rate and rhythm; evidence of defects in the

ventricle, such as predominance of either ventricle, spreading apart of the Q-R-S wave beyond the maximal normal of .10 seconds, thickening or notching in any part of the waves of the Q-R-S group, abnormalities of the P wave, such as the inversion seen as an effect of digitalis or other poisons affecting the heart muscle.

THE EXERCISE TEST

Tried in the fire of experience in sifting out the unfit among the United States recruits in the recent war, the exercise test was not found wanting. Its simplicity and lack of requirement of apparatus make it most desirable. The pulse rate is counted after the subject has been quietly seated for a few minutes. Then a measured amount of work is performed. This may be one hundred hops or repeatedly stepping upon a chair or but a few arm flexions—depending upon the safe capacity of the individual. The work performed should make a genuine demand upon the subject's capabilities. The pulse rate is counted immediately after exercise and again after two minutes of rest. In the absence of disease of the lungs or gross disease elsewhere, or of fatigue, the pulse rate in a young individual in good physical trim after one hundred hops should not be accelerated more than 20 beats per minute and should, within two minutes after stopping the exercise, be within 5 to 10 beats of the previous resting rate. Dyspnea should not be marked. Modified to suit individual needs of patient or physician, this test is the most practical of all for the practitioner.

The ideal test of circulatory function should take account of all possible factors. It should include the resting pulse rate, the standing pulse rate, the rate after exercise, the time required for return to resting normal rate after exercise and after change in posture; such respiratory factors as the vital capacity, the minute volume of pulmonary ventilation, the pressure gradient of carbon dioxide in the blood entering and leaving the lungs, the basal metabolic rate, the electrocardiogram—all this in addition to the time-tested physical examination and history.

With all this data complete in a given case, would we, even then, be in a position accurately to predict or measure

the capacity of a heart? We would be nearer but not at the goal. Such elusive factors as neuromuscular fatigue, psychic states, endocrine balance, are to most of us imponderables of weight but not weighable. The processes of the living being are too complex to compass with the precise limits of mathematical formulas. Desirable as the attempt always is, an attitude of inquiring skepticism is safest in the presence of claimed achievement.

POINTS FOR GRADING CARDIOVASCULAR CHANGES (AFTER SCHNEIDER)

A. Reclining Pulse Rate

Rate	Points
50– 60	3
61– 70	3
71– 80	2
81– 90	1
91–100	0
101–110	−1

B. Pulse Rate Increase on Standing

0–10 Beats, points	11–18 Beats, points	19–26 Beats, points	27–34 Beats, points	35–42 Beats, points
3	3	2	1	0
3	2	1	0	−1
3	2	0	−1	−2
2	1	−1	−2	−3
1	0	−2	−3	−3
0	−1	−3	−3	−3

C. Standing Pulse Rate

Rate	Points
60– 70	3
71– 80	3
81– 90	2
91–100	1
101–110	1
111–120	0
121–130	0
131–140	−1

D. Pulse Rate Increase Immediately after Exercise

0–10 Beats, points	11–20 Beats, points	21–30 Beats, points	31–40 Beats, points	41–50 Beats, points
3	3	2	1	0
3	2	1	0	0
3	2	1	0	−1
2	1	0	−1	−2
1	0	−1	−2	−3
1	−1	−2	−3	−3
0	−2	−3	−3	−3
0	−3	−3	−3	−3

E. Return of Pulse Rate to Standing Normal after Exercise

Seconds	Points
0– 60	3
61– 90	2
91–120	1
After 120: 2– 10 beats above normal	0
After 120: 11– 30 beats above normal	−1

F. Systolic Pressure, Standing Compared with Reclining

Change in mm.	Points
Rise of 8 or more	3
Rise of 2–7	2
No rise	1
Fall of 2–5	0
Fall of 6 or more	−1

What, then, is the practical conclusion of the whole matter? What will serve the practitioner as a rapid and fairly accurate test of circulatory efficiency? In addition to a developed clinical judgment and the information derivable from the ordinary history and physical examination, the simple exercise test will serve. While aware of its limitations, the observation of the acceleration of the pulse on a definite amount of exercise and the time required for a return to the previous resting rate will satisfy ordinary clinical requirements. Should a higher degree of precision be desired, Schneider's system of rating is to be recommended. The special student may go further and adopt any or all of the more elaborate methods mentioned. The more factors he takes into account, the better. Always, however, he strives for the unattainable—an exact and thoroughly reliable test of circulatory efficiency.

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HYPERTENSION AND HYPERGLYCEMIA*

W. W. Herrick, M.D.

THE association of hypertension and hyperglycemia has attracted the attention of a number of clinical observers. In 1910, Neubauer[1] noted this and offered the unproved theory that excessive activity of the suprarenals was the underlying factor. In this country, O'Hare[2] first established the fact of a decline in tolerance for carbohydrate in certain examples of high blood pressure. He offered the theory that sclerosis of the arteries of the pancreas might be the pathologic background of the condition. Pearce and Keith[3] suggested that, because a diseased kidney is unable to utilize the ordinary amount of sugar brought to it by the blood, diminished sugar consumption results, with increased accumulation of this substance in the blood stream. Meyers and Killian[4] noted the increase of the diastatic activity of the blood in examples of nephritis, and expressed the idea that this might account for the hyperglycemia often noted in such cases. Härle,[5] in a study of a series of cases of hypertension, failed to discover any exact parallelism in the curves of blood pressure and blood sugar. He found that real hyperglycemia was rare in cases with definite kidney lesion and hypertension. However, in one-fourth of the cases of hypertension without apparent kidney lesion, there was definite hyperglycemia. In another fourth, the blood sugar was at the upper limit of the normal. Härle concluded that hypertension and hyperglycemia are not the common result of increased activity of the chromaffin system. Botti[6] found that, in the presence of hypertension, blood sugar is increased and sugar tolerance lessened. He states that assimilation of carbohydrates may be impaired through delayed metabolism, lessened functional capacity of the liver, or disturbance of the general circulation. He could establish no relation between

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the degree of hypertension and the level of sugar in the blood. Janeway[7] noted a tendency to hypertension in elderly patients having diabetes with arteriosclerosis. Rosenbloom,[8] in a study of the blood pressure in diabetes, concluded that in the average case the blood pressure tends to be below normal. However, when arteriosclerosis or nephritis is present, the blood pressure is often elevated. Recently, Kylin[9] has described the association of lowered carbohydrate tolerance with hypertension. He makes further mention of the increase of uric acid in the blood in cases of this type, and states that cases characterized by hyperglycemia, hyperuricemia and hypertension belong in the group of essential hypertonias rather than in that of the diabetics.

PERSONAL OBSERVATION

Observation of the association of high blood pressure and increased concentration of glucose in the blood carried out during the last three years has led to the opinion that the majority of the cases belong in a quite definite group characterized by the four cardinal symptoms: hypertension, hyperglycemia, obesity and arteriosclerosis. While it does occur, it is rare that hyperglycemia is found in the thin person with hypertension.

Six typical examples of the symptom group set forth above are presented in the accompaning charts. These were ambulatory, office patients, who were observed over periods of from one to three years. The age of these patients was between fifty and sixty-four. Three were men and three were women. All were overweight and exhibited symptoms of cardiovascular strain, varying from dyspnea on exertion to anginal attacks or circulatory stasis. All had for some time prior to this study taken a diet from which meat was largely or entirely excluded, and had, in consequence, eaten more than an ordinary amount of carbohydrate. In two cases, there was an increase in the uric acid of the blood. The chlorids of the blood exceeded 5 gm. per liter in only one instance. In no case was the urea nitrogen above 20 mg. in 100 c.c. of blood. Arteriosclerosis was demonstrable in the retina in 4 of the cases.

The clinical management of this group may be briefly summarized. The patients were allowed to go about their ordinary concerns with no restriction other than the avoid-

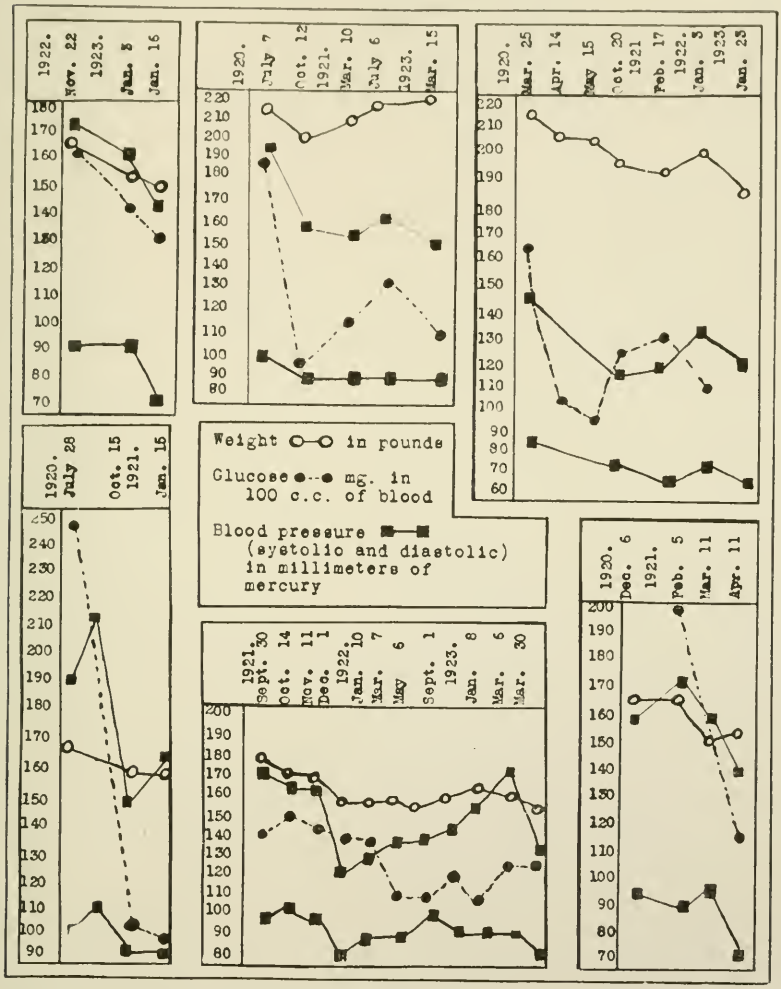

FIG. 38. Relation of systolic and diastolic blood pressure, weight and blood sugar.

ance of undue fatigue and effort, and, in addition, a modified diet. Such factors as physical rest, release from immediate pressure of the burdens of business or family, which make

data on blood pressure obtained under institutional conditions so misleading, are, therefore, not to be taken into account here. The diet prescribed contained about 1,600 calories, thus distributed: protein, 85 gm.; carbohydrate, 125 gm.; fat, 80 gm. In most instances, so strict a diet with its relatively high protein was followed for periods of from five to ten days with intervals of from one to two days during which the patient "broke training." If satisfactory decline in weight did not result, on every fifth or seventh day a limited milk diet was enforced. As will be noted, all patients lost weight. In all, both the systolic and the diastolic blood pressure declined appreciably, and in general remained below the initial point so long as the regimen was carried out. With the decline in weight and in blood pressure, there was an expected improvement in the cardiovascular symptoms, with corresponding increase in comfort.

COMMENT

In our description of the hypertonias, we separate from among the examples of hypertension that are associated with other definite conditions, such as kidney insufficiency, aortic leakage, toxemias of pregnancy, thyroid disturbances and increased intracranial pressure, a group without other recognized clinical association, the group we call the essential hypertonias. As clinical study develops, these so-called essential hypertonias will doubtless be further subdivided for purposes of clinical description and management. I would suggest as a tentative subdivision the type of case described, that characterized by the symptom group hypertension, hyperglycemia, obesity and arteriosclerosis.

While such speculative conditions as excessive activity of the chromaffin system, or sclerosis of the arteries of the pancreas, may well be in the background, in not a few of these patients one can trace possible etiology of the hyperglycemia and associated conditions to faulty and ill-balanced diet. It is still a matter of tradition and practice among not only the laity, but also perhaps a majority of the profession, to prohibit or limit the amount of protein food taken by the patient when hypertension is present. Since the amount of fat

that one can comfortably take is limited, protein deprivation leads directly to an increase and excess in carbohydrate intake. So much has been said and so little proved in respect to the dangers of protein food that the possible dangers of overfeeding with carbohydrate have had scant consideration.

What are the consequences of an ill-balanced diet with an excess of carbohydrate in a person in middle life with hypertension? If tolerance for carbohydrate is below the normal, there is certain overstrain of the pancreas and a tendency to the development of diabetes. There is also the almost certain result of increase in weight. In addition to these two results, which are scarcely debatable, there are two further possible consequences: one is an increasing tendency to arteriosclerosis; another, a rise in blood pressure. There is considerable ground for argument in favor of the view that arteriosclerosis and hyperglycemia are not mere casual associates. Even in juvenile diabetes, arterial thickening is extremely common. In the diabetes of later life, arteriosclerosis is constant. The happy effect of the control of hyperglycemia in cases exhibiting such arteriosclerotic complications of diabetes as gangrene and retinitis is scarcely disputed. However, I know of no experimental work on the relation of hyperglycemia and arteriosclerosis. Arguments favoring such a view are based solely on clinical observation. In the clinical type being considered—that characterized by hypertension, hyperglycemia, obesity and arteriosclerosis —the relation of hypertension to hyperglycemia is probably indirect. In this group, reduction of the blood sugar and its maintenance at or about normal, is, in my experience, quite constantly followed by reduction in blood pressure. It is probable that this is not a direct cause and effect, but is a consequence of the reduction in bulk of body which quite constantly follows the dietary regulation of high blood sugar in the obese, hypertonic patient. Rose and others have shown that decline in weight is almost always accompanied by decline in blood pressure, particularly when this has previously been high.[10]

The symptoms of cardiovascular strain that were universal in this group of obese patients having hypertonia with hyperglycemia were very favorably influenced by the decline

in weight attending the decline in hyperglycemia. Effects of this kind are probably due to reduction in body bulk, reduction in volume of circulating fluid, reduction in total metabolism, and possibly, as will be discussed elsewhere,[11] to alteration in concentration or distribution of some of the crystalloids of the blood. It has been my experience that those exceptional persons who are not overweight, but who have nevertheless a hypertension and hyperglycemia, do not show reduction in blood pressure by a regimen that brings the blood sugar down to a normal level and keeps it there.

It would, therefore, seem that the observations of Botti and Härle are substantially correct, and that there is no exact parallelism between the curves of blood sugar and the curves of blood pressure. The suggestion of Mosenthal,[12] that the decline in blood pressure, observed to follow reduction in blood sugar in cases of the character discussed, is probably the result of undernutrition resulting in loss in weight, is probably correct. In view of this apparent fact, the observation of the blood sugar in such cases might appear an unnecessary elaboration. The weight alone might seem an adequate guide in treatment. With this I do not agree. In patients of the type considered, resolution is often as flabby as tissue, and the physician needs every possible argument to enforce his decrees. The necessity of lightening the burden on the cardiovascular system can be stressed. If, in addition, the threat of diabetes can be held over the head of the patient, there is added argument for reduction in weight. The level of blood sugar is a useful guide in diet. Further, the reduction in weight of the obese person with hypertension plus hyperglycemia is a much simpler and easier matter than the reduction in weight of a similar type of patient with a normal or low blood sugar. With this more complete knowledge, the therapeutic problem can be approached with a vigorous certainty, which adds to the physician's influence. The immediate improvement in the general well-being of these patients, and the quick relief from the annoying symptoms of cardiovascular strain that follow the loss of a few pounds, are a convincing argument to the intelligent patient. If both physician and patient realize that not alone is obesity being fought, but diabetes and arteriosclerosis,

with its consequences, both can realize that the attempt is more than worth while.

CONCLUSIONS

1. Hyperglycemia is present in a considerable number—from 10 to 30 per cent—of examples of arterial hypertension.

2. It appears to be more common when high blood pressure is not associated with obvious disease of the kidney.

3. This association of hyperglycemia and hypertension is most common in those who are obese and inclined to show arteriosclerosis.

4. The cause of the hyperglycemia of hypertension is unknown. Plausible but unproved theories are: overactivity of the chromaffin system; sclerosis of the arteries of the pancreas, and increased diastatic activity of the blood. An undoubted cause in some cases is excessive use of carbohydrate food, the result of unwise restriction of protein.

5. Prolonged hyperglycemia may tend to cause arteriosclerosis and enhance blood pressure.

6. The reduction of blood sugar to a normal and its prolonged maintenance at a normal level in the type of cases considered is generally followed by significant fall in blood pressure.

7. This fall in blood pressure is probably due to the loss in weight which results from restricted diet.

8. Weight and blood sugar are valuable guides in the treatment of the obese person with hypertension.

9. In hypertensive cases in which the patient is overweight, carbohydrate is probably far more dangerous than protein. The latter should not be restricted unless incompetence of the kidney for the products of nitrogenous catabolism is demonstrated.

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A CASE OF CEREBELLAR ABSCESS WITH OPERATION AND RECOVERY*

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WE wish to report in this paper, a case of an abscess in the left cerebellar lobe in a child, the abscess having been successfully localized and drained, and ultimate recovery resulting. We believe this case to be of sufficient rarity to report in some detail from the standpoint of diagnosis, prognosis and treatment.

The child, a girl of eight years, was admitted to Roosevelt Hospital on June 28, 1923, the mother giving the following history: Eight weeks previously she had had scarlet fever, at which time the left ear began to discharge. This continued through her illness. It was described as a rather thick purulent discharge. Two years previously, in 1921, she had had a left mastoid operation. This old mastoid scar, soon after the left-ear discharge, "became puffy" and the child complained of a very severe headache, chiefly occipital. The skin over the site of the old mastoid operation was incised. Pus was obtained, attended by complete relief from the headache. This wound discharged for about two weeks, and the ear discharge became less and less. The child had complete relief from the headaches for about three days, when these returned with increasing severity. Aspirin was given, which mitigated the pain for about six hours. She went through her scarlet fever well, and desquamation began about this time. Her chief complaint was the headache, which was becoming more and more severe, aspirin now having no effect. On June 7th, which was four weeks after the onset of the headache, she

* This paper was written especially for The Roosevelt Hospital Report, 1924.

began to vomit. This became intractable at times, and projectile in type, and would occur even when the stomach was empty. However, it is of interest to note that she would have a good day every other day with entire relief of these symptoms. On these days she would sit up and take food. This periodicity, of headache and vomiting one day and absence of these symptoms the next, continued until her admission to the hospital.

Her past history is as follows. Her birth weight was 4½ lbs. and she was nursed for nine months. At two years of age she had a left otitis media, and at five years, measles. At six years of age (in 1921) she had a left mastoid operation. A note made on June 13th (two weeks prior to the operation) says: "Lies with head retracted and legs drawn up. Sleeps most of the time. Scaphoid abdomen. Pupils equal and react promptly to light. No Kernig or Babinski. Vomited twice during the day." Another note, made two days later, says: "Headache continues. Head is retracted. Vomited once." It is of interest to note that the temperature was normal and the pulse regular and not retarded. The urine examination was negative. Shortly after this a lumbar puncture was done, with the following findings:

Pressure considerably increased
Fluid clear
Albumen + (2 mm. ring)
Fehling's reduced.
Globulin 1 +
Small lymphocytes 3
Polymorphonuclears 2
No tubercle bacilli found
Culture negative.

After admission to the hospital a von Pirquet was done and was markedly positive. The blood showed a white blood cell count of 9,500 with the polymorphonuclears 54 per cent and the lymphocytes 46 per cent. These findings, with the rest of the picture, rather suggested a tuberculous meningitis. An examination of the eye-grounds was negative and an *x*-ray of the skull did not help to confirm our diagnosis of a brain abscess. The report of the roentgenolo-

gist is as follows: "There are no findings, either direct or indirect, of a brain abscess. The left mastoid cells are not shown."

Dr. McKendree was called in consultation at this time and his neurological examination follows:

"Projectile vomiting of seven weeks' duration; severe headache for two weeks: marked nystagmus in lateral positions, with the rapid jerk to the left, pupils normal in contour and response to light, and convergence. The fundi were entirely negative. There were no ocular palsies. No rigidity of the neck, and no Kernig. The deep reflexes were all present and equal. The abdominal reflexes were present on both sides. No Babinski or modifications. In approximating the left finger to the nose there was definite swinging ataxia. Adiadokokinesis was present in the left upper extremity. There was no non-equilibratory disturbance of any kind in the right upper extremity.

Diagnosis. Abscess of left cerebellar lobe.

With the localization of the abscess in the region of the left cerebellar lobe, it was agreed that an operation should be done as soon as possible. The child was becoming progressively worse, emaciation was extreme, due to the intractable vomiting, and headache was now an almost constant symptom, causing sleepless nights and unrelieved by opiates. This operation was done on June 29, the day after admission to the hospital. Gas and ether anesthesia were used.

Dr. Howell's report of the *surgical procedure and after-treatment* follows:

"On account of the extreme illness of the child, and the probable location of the disease close to vital centers, it was deemed necessary to move along with the various stages of the operation with as little delay as possible, doing a plastic closure perhaps at a subsequent time.

"On exposing the mastoid region through the former line of incision, the old cavity was found considerably contracted and filled with spongy, new-formed bone. To give a more complete field for observation, knowing the possibilities of error in this type of case, a radical mastoidectomy was done. As we worked toward the attic the bone seemed softer, so this was followed up and the roof separating the middle fossa

chipped off to see the condition of the dura over the temporosphenoidal lobe. This was regarded as being normal. Next, the labyrinth was examined from the inner tympanic wall aspect, and the horizontal semicircular canal eminence. No suspicious spots were discovered, and so, coupled with the fact that at our examination we elicited some hearing, we were safe in presuming we had no purulent labyrinthitis to deal with. Likewise, the lateral sinus, as evidenced by an intact bony plate, was unaffected, so that if we were to find a cerebellar abscess, it must have occurred by way of the lymphatics or blood stream. Accordingly, our mastoid wound was enlarged by a horizontal incision posteriorly, the soft parts and periosteum elevated and the occipital bone behind and below the lateral sinus trephined and enlarged with bone forceps. The underlying dura was found to be under great pressure, but with less pulsation over the central exposed region than one would ordinarily expect. By the use of an exploratory needle about 1¼ in. deep, a thin fluid, at first cloudy but becoming immediately purulent, was recovered, verifying the diagnosis.

"A very small crucial incision was made in the dura, and a pair of narrow anatomical forceps introduced in the same direction as the needle, but gradually penetrating a little deeper, thus giving exit to 2 or 3 dr. of bad-smelling, thin, purulent fluid. We were now apparently in a cavity measuring roughly 1 by ¾ in. The dural opening was next enlarged sufficiently to receive two rubber tubes, No. 12, French size. These were stitched to the skin and dressing placed around them, while the mastoid wound was packed as in an acute case. I made no attempt to do a plastic closure at this time, though, all things considered, the condition of the child was fair, the pulse being 160 instead of 90, as at the commencement of the operation.

"The entire time in the operating room was 1½ hrs.

"A *culture report* from the laboratory showed that the pus from the abscess cavity was sterile, a finding which is not at all unusual in such cases.

"I wish to express here my thanks to Dr. Robert E. Buckley, whose assistance was of greatest value.

"The condition of the child next morning was extraordinarily good: pulse 124, bright, though very weak of course, and headache completely gone, nor has she had any return of it during her entire convalescence. There was considerable oozing from the wound, necessitating change of outer dressings twice a day for a week, less often after that. All packing was out of the mastoid wound in a week and lightly replaced. The tubes were retained a month, then one of them was removed, and the other shortened from time to time as the abscess cavity closed in; late in August it was removed entirely.

"The child was allowed in a wheel chair July 25th, and was discharged, healed, on September 7th. She has gained greatly in weight and general health: in fact, she looks like a normal, well-nourished girl. Her left arm is nearly as strong as her right. There is still a slight discharge from the middle ear. I have seen her once a week since she left the hospital, and she has felt so well that she was permitted to begin school on October 1st. On October 20th, she reported a postauricular abscess, but without pain. This was opened and ¾ dr. of pus was evacuated. This healed entirely within a week, and the report is that she is again entirely well. The last report from this child was on November 1, 1924, one year and four months after the operation. She was in splendid health, gaining in weight and going to school. The slight left facial weakness which she had following the operation had entirely cleared up."

INFLUENCES OF EXTRARENAL FACTORS ON THE RENAL FUNCTIONAL TEST MEAL*

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FACTORS INFLUENCING TEST MEALS

SEEKING to investigate renal function in both healthy and diseased kidneys in terms of their response to their most accustomed stimulation, Hedinger and Schlayer[1] studied their reaction to a twenty-four-hour standard diet. Mosenthal,[2] continuing this method, revised their procedure and made it somewhat more adaptable to private practice and non-hospital patients. His dietary contained about 13.4 gm. of nitrogen, 8.5 gm. of salt, and 1,760 c.c. of fluid, including a fair quantity of diuretic materials in the form of purins. The twenty-four-hour diet was given in three meals: at 8 A.M., 12 M. and 5 P. M. The urine was collected at two-hour intervals from 8 A.M., to 8 P.M., and a night specimen from 8 P.M. to 8 A.M. of the following day; but no three-day fixed diet was demanded preceding the last day, as was suggested by Hedinger and Schlayer. Furthermore, Mosenthal felt there was no essential need for following out exactly the kind of meal he outlined, if only the subject partook of his three accustomed meals a day, took no food or drink between them, and followed the directions given for the collection of urine.

This procedure proved to be, in his opinion, an excellent one for the test of renal function. His normal subjects returned two-hour urinary specimens that varied 10 points in specific gravity between the highest and the lowest (later 9 points were accepted as the minimum normal variation). The night urine was 1.018 or more in specific gravity with its nitrogen concentration above 1 per cent and a total volume of 400 c.c. or less. The quantitative excre-

* From Harriman Research Laboratory and Pathologic Laboratory of The Roosevelt Hospital. Reprinted from *Arch. Int. Med.*, March, 1918.

tion of nitrogen, salt and water approximated the intake. With a renal function impairment, the earliest change appeared in the night urine; the quantity increased, the specific gravity lowered and the nitrogen concentration was reduced. Severe functional derangement manifested itself by a much lowered and constantly fixed specific gravity in all specimens and a diminished output of nitrogen, salt and water. Later, Mosenthal and Lewis[3] in comparing several of the approved tests for renal function, namely, the phenolsulphonephthalein, nonprotein nitrogen and urea content of the blood, Ambard coefficient of urea excretion and the test meal, found the latter to be the most sensitive, in that it was relatively the first to disclose any degree of renal inefficiency.

Aware of the possibilities of the influence of extrarenal factors on the test-meal reaction, we undertook to study the degree of uniformity of response to the test meal by the same individual, the extent to which a lack of such uniformity might interfere with unqualified interpretations of the results, and to disclose, if possible, extra renal factors that may have operated to produce such variations in reactions. All our subjects were persons going about their duties and leading their accustomed lives. They were fed a standard diet, approximating that outlined by Mosenthal at a special diet kitchen, associated with the laboratory of Roosevelt Hospital. Each took the test meal for two, three or more days, usually consecutively, and carried out with care the instructions as to the collection of urine and abstinence from food and drink between meals.

As concluded by Mosenthal, and too, as a result of our experiments (which already include over 200 test meals) variations in the specific gravity of the two-hour specimen of urine, and the volume and character of the night specimen, appear to be an index to the state of renal functions, as elicited by the test. The reaction of the kidney to the stimulus of the food given in the test meal truly represents the reaction for which the test was conceived and shows the actual renal factors involved in the reaction. Influences from other sources serving to affect significantly the specific gravity variations, the volume or the nitrogen concentration of the night

specimen must be looked on as complicating extrarenal factors. The variations in specific gravity of the two-hour urinary specimens are functions of both the volume of fluid and amounts of solids excreted during each period, and it is quite apparent that extrarenal influences on one or the other of these factors can influence the periodic specific gravity variations.

As for the excretion of water, the skin and lungs as well as the kidneys are excretory organs. The loss of water from the body surface is subject to the physical laws which govern water evaporation, and serves definite purposes. Hence the influence on such fluid loss of atmospheric temperature, humidity and rate of air circulation. This loss of water is a vehicle for the dissipation of body heat and is a factor in the mechanism for regulation of body temperature. The remarkable constancy of body temperature in health stamps the mechanism of its regulation, and thus the operation of its several factors, as exceedingly persistent. It is thus accorded priority over less persistent body functions, and fluid supplied the kidneys for excretion must be secondary to the demand made at that time on the body fluids by the temperature-regulating mechanism.

Investigating with the calorimeter the question of water excretion, Rubner[4] found that at a constant atmospheric temperature the water loss by skin was directly proportional to the relative humidity; an increase of water loss with an increase of atmospheric temperature; and further, that about 21 per cent of body heat produced was dissipated by water evaporation. Gephart and DuBois[5] estimated the amount to be in the neighborhood of 24 per cent. Wolpert and Peters,[6] studying the daily curve of water excretion through skin and lungs, found that it was not influenced by the time of day, as such, but was at a minimum during the late night hours or the day hours of sleep. In other words, it was at a minimum when metabolism was at a minimum. Further, the intake of food had no influence on the curve of excretion. They found an average excretion of 70 gm. of water per hour at 24 C., and 65 per cent relative humidity when the air was still. Laschtschenko,[7] investigating the effect of water intake on water excretion from skin and lungs, found that it exerted

no influence whatever. To summarize then: water loss by skin and lungs takes precedence over excretion by kidney; it is lowest when metabolism is lowest; it is not influenced by the intake of food or fluids and under ordinary circumstances must be nearer a liter (in the active man) than the 400 c.c. allowed by Mosenthal.[2, 8] The fluid supply to the kidney consequent to such a preferential demand by the skin is gauged by the condition of water balance of the body, which, in turn, is manifestly influenced by the water intake.

The reactions of Subjects S. and B. given in Tables I and II, illustrating the tendency of the responses of most of our subjects to the test diet when taken for a few consecutive days, show a tendency toward concentration and reduction in the range of variations in specific gravity of the two-hour specimens. The total fluid output fell steadily from day to day (2, 7, 17, Table I excepted) and the sodium chlorid elimination fell likewise. The nitrogen excretion was not definitely interfered with by the progressive tendency toward oliguria. This change in response of the kidney appears in spite of the identical stimulus to the kidney of food and fluid intake. In general terms, such reactions as these are explained as due to an effort on the part of the body to prevent depletion of its fluids in order to keep constant the concentration of its solids. It is difficult to explain what factors operated in any particular day's reaction to compel conservation of body fluids. This conservation might have been due to excessive preferential demand for water by the skin, resulting from a marked increase in metabolism or exposure to atmospheric temperature and relative humidity most favorable for water evaporation. On the other hand, the volume of fluid ingested may have been too low for the subject, or the solid intake too high. When these latter factors are operating the concentration and fixation of specific gravity would become progressively more marked as the test days went on, as illustrated by the cases just outlined; then again, the test meal might have been given at a time when the tissues were in a state of fluid depletion. In all events, it appears that the water balance of the body is in a state of apparently fine adjustment in the healthy individual, and this balance the body

TABLE 1

SHOWING URINARY REACTION ON A TEST DIET

Student S., aged 22; laboratory assistant in good health

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
12/6/16						
8–10 A.M.	140	1.022				
10–12 M.	265	1.020				
12– 2 P.M.	420	1.014				
2– 4 P.M.	354	1.012				
4– 6 P.M.	146	1.018				
6– 8 P.M.	194	1.016				
Total day	1,519	.....	7.10	0.47	11.4	0.75
Total night, 8 P.M.–8 A.M.	340	1.026	3.69	1.00	3.35	0.99
Total 24 hours	1,859	.....	10.79	....	14.75	
2/5/17						
8–10 A.M.	105	1.022				
10–12 M.	200	1.020				
12– 2 P.M.	156	1.022				
2– 4 P.M.	154	1.023				
4– 6 P.M.	187	1.021				
6– 8 P.M.	242	1.016				
Total day	1,044	.....	.....	....	7.10	0.68
Total night, 8 P.M.–8 A.M.	540	1.018	.....	....	3.60	0.66
Total 24 hours	1,584	.....	.....	....	10.70	
2/6/17						
8–10 A.M.	80	1.020				
10–12 M.	135	1.021				
12– 2 P.M.	330	1.016				
2– 4 P.M.	180	1.024				
4– 6 P.M.	130	1.025				
6– 8 P.M.	175	1.022				
Total day	1,030	.....	8.6	0.83	6.7	0.65
Total night, 8 P.M.–8 A.M.	380	1.024	2.7	0.72	2.5	0.65
Total 24 hours	1,410	.....	11.3	....	9.2	
2/7/17						
8–10 A.M.	105	1.022				
10–12 M.	175	1.022				
12– 2 P.M.	185	1.024				
2– 4 P.M.	165	1.024				
4– 6 P.M.	120	1.026				
6– 8 P.M.	335	1.015				
Total day	1,085	.....	12.0	1.1	7.1	0.65
Total night, 8 P.M.–8 A.M.	610	1.016	6.8	1.1	4.2	0.70
Total 24 hours	1,695		18.8		11.3	

strongly seeks to maintain. Nor is it difficult to appreciate how the effort to preserve such a balance will, in a great measure, influence the maximum specific gravity in the test-meal reaction, as well as the maximum variation therefrom.

TABLE I

SHOWING URINARY REACTION ON A TEST DIET — *Continued*

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
2 8 17						
8–10 A.M.	60	1.025				
10–12 M.	108	1.026				
12–2 P.M.	150	1.023				
2–4 P.M.	126	1.025				
4–6 P.M.	100	1.027				
6–8 P.M.	131	1.025				
Total day	681	.....	4.8	0.70	2.2	0.66
Total night, 8 P.M.–8 A.M.	325	1.025	2.5	0.77	2.1	0.65
Total 24 hours	1,006	.....	7.3	....	4.3	
2 9 17						
8–10 A.M.	72	1.027				
10–12 M.	60	1.028				
12–2 P.M.	98	1.029				
2–4 P.M.	94	1.029				
4–6 P.M.	120	1.029				
6–8 P.M.	132	1.025				
Total day	576	.....	5.1	0.89	4.1	0.70
Total night, 8 P.M.–8 A.M.	400	1.027	5.1	1.27	2.6	0.60
Total 24 hours	976	.....	10.2	....	6.7	

The subject complained very much of thirst the last two days of the test. On the single day (Dec. 6th) there was a variation of specific gravity from 1.012 to 1.022, 10 points. Beginning with Feb. 5th, the variations between maximum and minimum for five consecutive days are 7, 9, 11, 4 and 4 points.

Table III discloses the interesting fact that with the successive reduction of the total twenty-four-hour volume of urine there was a tendency toward a percentile increase of the night volume, or, in other words, a tendency toward a constancy of night volume in spite of successive diminutions in daily total volumes. It is to be recalled in this connection that water loss from the skin is at a minimum during the sleeping hours and consequently there is relatively more

water available to the kidney for excretion during that time. An extrarenal factor of a different order which will be men-

TABLE II

URINARY REACTIONS ON A TEST DIET

Subject B., aged 25; physician on house staff in good health

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
2/13/17						
8–10 A.M.	120	1.026				
10–12 M.	160	1.025				
12– 2 P.M.	216	1.024				
2– 4 P.M.	128	1.020				
4– 6 P.M.	104	1.029				
6– 8 P.M.	85	1.031				
Total day	813	.....	6.7	0.82	6.1	0.75
Total night, 8 P.M.–8 A.M.	303	1.029	3.8	1.2	2.1	0.68
Total 24 hours	1,116	.....	10.5	....	8.2	
2/14/17						
8–10 A.M.	82	1.028				
10–12 M.	102	1.026				
12– 2 P.M.	109	1.029				
2– 4 P.M.	120	1.028				
4– 6 P.M.	99	1.030				
6– 8 P.M.	70	1.028				
Total day	582	.....	6.3	1.1	7.9	1.3
Total night, 8 P.M.–8 A.M.	276	1.031	3.9	1.4	1.0	0.36
Total 24 hours	858	.....	10.2	....	8.9	
2/15/17						
8–10 A.M.	74	1.029				
10–12 M.	55	1.030				
12– 2 P.M.	124	1.028				
2– 4 P.M.	70	1.029				
4– 6 P.M.	80	1.033				
6– 8 P.M.	49	1.031				
Total day	452	.....	6.1	1.4	3.4	0.74
Total night, 8 P.M.–8 A.M.	342	1.031	5.2	1.5	2.5	0.74
Total 24 hours	794	.....	11.3	....	5.9	

The specific gravity variations for the three consecutive days are 11, 4 and 5 points.

tioned later, however, may be the contributory cause in the test day of Feb. 7, 1917, of Subject S., where the night

volume equaled 56 per cent of the total twenty-four-hour volume. It is pertinent to recall in this connection the findings of Quincke,[9] who, in studying the urinary output of subjects who were not ill of nephritis, found that the average hourly output of the early morning hours (from 5 to 8 A.M.)

TABLE III

SHOWING PERCENTILE INCREASE OF NIGHT OVER DAY VOLUME

Date	Subject S.						Subject B.		
	12/6	12/5	2/6	2/7	2/8	2/9	2/13	2/14	2/15
Total day vol. c.c.	1,519	1,044	1,030	1,085	681	576	813	582	452
Total night vol. c.c.	340	540	380	610	325	400	303	276	342
Total 24-hr. vol., c.c.	1,859	1,584	1,410	1,695	1,006	976	1,116	858	794
Percentile ratio of total night to 24-hr. volume	18	34	27	36	32	41	27	32	43

was far greater than that for the twenty-four hours or the total night hours. To what extent, we may ask, did the minimum loss of water by skin and lungs during the night render possible the availability of fluids for the kidney at a time so removed from the last hours of water intake?

Mosenthal recognized the tendency toward a fixation of specific gravity at a high concentration in healthy subjects with oliguria, and allows for it in a measure by taking the highest specific gravity of the day as a basis for estimating the normal variations in the urine of subjects taking the test meal.

It is well known that exposure to cold and chilling of body surface induce an increased flow of urine. The causes of this phenomenon are apparently not identical in every instance and probably vary in particular cases. Several factors may have operated in the production of the diuresis. In the first place, the chilling of the body surface may have caused a constriction of surface vessels, secondary to which splanchnic dilatation to some degree, including renal vessels, might occur. Secondly, the peripheral vasoconstriction shuts off water loss by evaporation from the skin, thereby allowing an increase of fluids at the disposal of the kidney. Thirdly,

one must consider the possibility of the response of the kidney through a nervous mechanism with the stimulation of the skin by cold as the source of the afferent impulse.

Jungman [10] demonstrated by cerebral stimulation in animals that this nervous mechanism was not merely the expression of a vasomotor reaction, as shown by the character of the urine during the diuretic period. This latter fact had not been studied by Ashner and Bechterew, who, prior to Jungman, had investigated diuresis produced by cerebral stimulation. Jungman, keeping his animals on a fixed diet and comparing the urine of control days and immediate foreperiods with the period immediately following cerebral stimulation, found that the urine of the diuretic period contained an increase of sodium chlorid, due both to an increase in volume and in concentration, this at times reaching tenfold that of the control period and even exceeding at times the chlorid concentration in the blood. Furthermore, separate specimens of urine drawn off at different times during a single diuretic period showed the volume and sodium chlorid concentration to be mutually independent. The absolute nitrogen output was found to be fairly constant. All these findings were independent of water intake, which was determined by control experiments. Jungman, on the basis of these results, suggested that the stimulation of the renal epithelium might be a factor, and that vasomotor reaction was not the only phenomenon to explain the result of this nerve stimulation.

The reactions of Subject O., as given in Table IV, show how chilling of the body surface can affect the test-meal reaction.

On the first day, Feb. 13, 1917, the heating apparatus was shut off in the laboratory, and Subject O., feeling uncomfortably cold all day, passed a total day volume of 1,864 c.c. as against 847 c.c., 1,103 c.c. and 672 c.c. on the three subsequent days. With this as the probable extrarenal factor, the diuresis was practically continuous all day, the specific gravity varying at the most 5 points, though the concentration was correspondingly lower. Again, on the night of the third test day, Feb. 15, 1917, after walking an hour and a half in the cold, he passed about 500 c.c. of his total night specimen of 790 c.c. at 10.30 P.M. For the four test meals,

TABLE IV

SHOWING HOW REACTION IS AFFECTED BY CHILLING OF BODY SURFACE

Subject O., aged 25; laboratory assistant in good health

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
2/13/17						
8–10 A.M.	286	1.017				
10–12 M.	238	1.015				
12–2 P.M.	322	1.020				
2–4 P.M.	310	1.020				
4–6 P.M.	430	1.017				
6–8 P.M.	278	1.016				
Total day	1,864	.....	9.30	0.50	14.1	0.76
Total night, 8 P.M.–8 A.M.	630	1.019	5.2	0.80	4.3	0.68
Total 24 hours	2,494	.....	14.5	....	18.4	
2/14/17						
8–10 A.M.	74	1.024				
10–12 M.	118	1.027				
12–2 P.M.	135	1.025				
2–4 P.M.	184	1.025				
4–6 P.M.	138	1.027				
6–8 P.M.	198	1.023				
Total day	847	.....	12.0	1.4	6.3	0.75
Total night, 8 P.M.–8 A.M.	280	1.029	4.8	1.7	2.0	0.70
Total 24 hours	1,127	.....	16.8	....	8.3	
2/15/17						
8–10 A.M.	50	1.025				
10–12 M.	194	1.020				
12–2 P.M.	133	1.020				
2–4 P.M	340	1.021				
4–6 P.M.	138	1.019				
6–8 P.M.	248	1.015				
Total day	1,103	.....	9.3	0.84	8.4	0.76
Total night, 8 P.M.–8 A.M.	790	1.016	5.6	0.70	6.0	0.76
Total 24 hours	1,893	.....	14.9	....	14.4	
2/16/17						
8–10 A.M.	72	1.026				
10–12 M.	98	1.024				
12–2 P.M.	125	1.025				
2–4 P.M.	163	1.020				
4–6 P.M.	86	1.027				
6–8 P.M.	128	1.029				
Total day	672	.....	9.2	1.37	5.1	0.76
Total night, 8 P.M.–8 A.M.	290	....	5.6	1.92	1.9	0.64
Total 24 hours	962	.....	14.8	....	7.0	

the absolute nitrogen elimination for the twenty-four hours was relatively constant, both in the total night and day specimens, and as a necessary corollary the nitrogen concentration varied inversely as the volume. The sodium chlorid concentration throughout the period was very constant; the increased volume not reducing, but showing rather a tendency toward increasing it. The sodium chlorid output varied considerably, therefore, with the fluctuations in the volume of urine. These urinary findings coincide with those of Jungman in the diuretic specimens, resulting from the stimulation of the fourth ventricle. The influence of cold must be considered; for it can interfere considerably with the correct interpretation of the test meal. Even as an influence for part of the day it will increase or decrease the maximum variation of the specific gravity, depending on whether the specific gravities of the specimens outside the period of its operation were high or low. At night, especially, if the room is cold and the subject happens to throw off some of the coverings during sleep, thus exposing the body surface, the urinary findings may be identical with those described by Mosenthal as the earliest signs of impairment of renal function. Influence on the renal nervous mechanism by emotional states could affect the reactions in a similar way.

Subject P., aged forty-four. Her symptoms had been headache, dyspnea and weakness. Hemoglobin 78 per cent; blood pressure 165/110; eyegrounds, slight arteriosclerosis. Phenolsulphonephthalein output, Feb. 14, 1917, 58 per cent in two hours. Blood picture, Feb. 14, 1917, nonprotein nitrogen 42, creatinin 0.96, uric acid 3.8 mg. per 100 c.c. The urine showed a faint trace of albumin and a few hyaline casts, with negative findings on several examinations.

Subject T., aged forty-five, had complained of occasional headache and dyspnea. Blood pressure 165/110. Blood picture, March 5, 1917, nonprotein nitrogen 28, urea 32, creatinin 1.5, and uric acid 4.0 mg. per 100 c.c. The urine showed a trace of albumin and many hyaline and granular casts.

Of the group of subjects with definite renal involvement we submit the reactions of two who, previous to the test, were on restricted diets for several months and who at the time of the tests were subjectively free of any symptom consequent to renal insufficiency. We are here afforded an opportunity to observe the effect of dietary treatment on renal function as evidenced by this test, and, what is more to our present purpose, the influence on the degree of relia-

TABLE V

REACTIONS OF SUBJECT P.

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
2/13/17						
8–10 A.M.	336	1.009				
10–12 M.	290	1.012				
12– 2 P.M.	285	1.011				
2– 4 P.M.	120	1.020				
4– 6 P.M.	134	1.017				
6– 8 P.M.	58	1.023				
Total day	1,223	.....	4.4	0.36	7.7	0.63
Total night, 8 P.M.–8 A.M.	240	1.023	2.4	0.99	1.6	0.68
Total 24 hours	1,463	.....	6.8	....	9.3	
2/15/17						
8–10 A.M.	25	1.030				
10–12 M.	65	1.020				
12– 2 P.M.	46	1.023				
2– 4 P.M.	74	1.020				
4– 6 P.M.	171	1.018				
6– 8 P.M.	58	1.025				
Total day	439	.....	4.3	0.98	3.2	0.73
Total night, 8 P.M.–8 A.M.	888	.....	4.1	0.46	6.5	0.74
Total 24 hours	1,327	.....	8.4	....	9.7	
2/16/17						
8–10 A.M.	71	1.019				
10–12 M.	130	1.017				
12– 2 P.M.	93	1.022				
2– 4 P.M.	90	1.018				
4– 6 P.M.	110	1.019				
6– 8 P.M.	71	1.027				
Total day	565	.....	4.5	0.79	4.1	0.73
Total night, 8 P.M.–8 A.M.	350	1.021	3.1	0.90	2.6	0.75
Total 24 hours	915	.....	7.6	....	6.7	
2/20/17						
8–10 A.M.	166	1.017				
10–12 M.	65	1.021				
12– 2 P.M.	82	1.020				
2– 4 P.M.	85	1.022				
4– 6 P.M.	128	1.022				
6– 8 P.M.	124	1.025				
Total day	650	.....	4.5	0.75	4.2	0.70
Total night, 8 P.M.–8 A.M.	590	.....	4.0	0.68	4.1	0.69
Total 24 hours	1,240	.....	8.5	....	8.3	

bility of the test-meal findings with the omission of the fixed diets for the several days preceding the test as suggested by Hedinger and Schlayer.

TABLE VI

REACTION OF SUBJECT T.

Date	Volume, c.c.	Specific gravity	Nitrogen		Sodium chlorid	
			Gm.	Per cent	Gm.	Per cent
3/5/17						
8–10 A.M.	40	1.024				
10–12 M.	36	1.028				
12– 2 P.M.	96	1.026				
2– 4 P.M.	46	1.024				
4– 6 P.M.	76	1.027				
6– 8 P.M.	90	1.025				
Total day	384	.....	5.5	1.4	4.0	1.05
Total night, 8 P.M.–8 A.M.	240	....	4.0	1.7	2.2	0.92
Total 24 hours	624	.....	9.5	....	6.2	
3/6/17						
8–10 A.M.	78	1.023				
10–12 M.	168	1.019				
12– 2 P.M.	164	1.021				
2– 4 P.M.	304	1.015				
4– 6 P.M.	114	1.014				
6– 8 P.M.	292	1.013				
Total day	1,120	.....	6.4	0.62	7.6	0.74
Total night, 8 P.M.–8 A.M.	495	.....	3.8	0.72	4.0	0.81
Total 24 hours	1,615	.....	10.2	....	11.6	
3/7/17						
8–10 A.M.	72	1.023				
10–12 M.	50	1.019				
12– 2 P.M.	98	1.023				
2– 4 P.M.	121	1.019				
4– 6 P.M.	76	1.022				
6– 8 P.M.	108	1.025				
Total day	525	.....	4.9	0.93	5.2	1.0
Total night, 8 P.M.–8 A.M.	670	.....	3.9	0.58	6.7	1.0
Total 24 hours	1,195	.....	8.8	....	11.9	

Though no specific effort was made to investigate the effect of a previous dietary, the response of Subjects P. and T. to the test meal add further data to the discussion of nitrogen

TABLE VII

SUMMARY

Name and date	Maximal specific gravity	Maximal variation	Night urine				
			Volume, c.c.	Specific gravity	Nitrogen per cent	Per cent above or below 400 c.c.	Per cent above or below 1% N concentration
Normal							
Subject S.							
12/6	1.022	10	340	1.026	1.0	− 15	0
2/5	1.023	7	540	1.018	....	+ 35	
2/6	1.025	9	380	1.024	0.72	− 5	−28
2/7	1.026	9	610	1.016	1.1	+ 53	+10
2/8	1.027	4	325	1.025	0.77	− 19	−23
2/9	1.029	4	400	1.027	1.27	0	+27
Subject O.							
2/13	1.025	8	590	1.015	0.86	+ 48	−32
2/14	1.027	4	280	1.029	1.7	− 30	+70
2/15	1.025	5	790	1.017	0.7	+ 98	−30
2/16	1.029	9	290	1.029	1.93	− 27	+93
Subject D.							
3/ 5	1.025	18	315	1.023	1.1	− 21	+10
3/ 6	1.021	14	210	1.027	1.2	− 48	+20
3/20	1.019	13	375	1.019	0.93	− 6	− 7
3/21	1.020	16	320	1.022	1.15	− 20	+15
3/22	1.023	19	285	1.025	1.3	− 38	+30
Chronic interstitial nephritis							
Subject G.							
3/14	1.021	7	460	1.013	0.74	+ 12	−26
3/15	1.023	8	668	1.015	0.84	+ 67	−16
3/16	1.030	5	618	1.021	1.20	+ 55	+20
Subject P.							
2/13	1.023	14	240	1.023	0.99	− 40	− 1
2/15	1.027	9	888	1.010	0.46	+112	−54
2/16	1.027	10	350	1.021	0.90	− 13	−10
2/20	1.025	8	590	1.015	0.68	+ 48	−32
Subject T.							
3/ 5	1.028	4	240	1.024	1.7	− 40	+70
3/ 6	1.023	10	495	1.015	0.76	+ 24	−24
3/ 7	1.025	6	670	1.017	0.58	+ 68	−42
Subject L.							
2/28	1.029	15	899	1.010	0.67	+125	−33
3/ 1	1.024	7	760	1.014	0.90	+ 90	−10
3/ 2	1.028	2	590	1.020	1.2	+ 48	+20

excretion in nephritics having difficulty with nitrogen elimination. They had been put on a diet low in nitrogen and high in fluids, drinking usually a gallon of water a day. This was continued until the test meals were given. The reactions for the first day appear comparatively normal in both, allowing for the results that follow oliguria in Subject T. In the successive test days, however, the findings correspond to the reaction of interstitial nephritics—an increased night volume, reduced nitrogen concentration (except that of Feb. 16, 1917, Table v). They show on all days, however, nitrogen retention. The absolute nitrogen outputs show a fair degree of constancy for each of the consecutive days, and an equal degree for the day and night specimens when their eliminations are separately considered. The constancy appears to be one of total rather than of percentile elimination. Thus, Subject T., having difficulty with nitrogen elimination, can concentrate nitrogen as high as 1.7 per cent in night specimens, and Subject P., as high as 0.99 per cent. Such variations in nitrogen concentration can appear, then, in the urine of individuals who have difficulty with nitrogen elimination, and it seems possible that a long-continued diet low in nitrogen and high in fluids might have enabled them to respond quite normally, for one day anyway, to the renal test meal, though no concomitant power for increased total nitrogen elimination is evident.

A fair index of the reliability of any judgment based on a single test-meal reaction in active individuals, healthy, or with slight, though definite, renal involvement, can be gathered from Table vii. Degrees of variations of specific gravity between maximum and minimum fluctuate markedly, and the variations do not necessarily diminish with the increase of maximum specific gravity, but may be quite the reverse (Subject D.). The night volumes, too, show decided fluctuations, varying, as in Subject O., from 98 per cent above 400 c.c. to 27 per cent below it on the following day. The nitrogen concentration of the night specimen shows a similar tendency to vary significantly above and below 1 per cent (Subject T.); and the higher nitrogen concentration may occur with the specimen of lowest specific gravity (Subject S., Feb. 7, 1917). Finally, the range of variation of the com-

posite test-meal reactions is quite sufficient to enable one, by selective comparison, to demonstrate at times, on the basis of the accepted method of interpretation, the better reaction for the poorer kidney.

SUMMARY

The kidney is called on during the course of a day to respond to many influences other than the stimulus of ingested food.

Such extraneous influences are extrarenal factors affecting the test-meal reaction.

Some of the factors we have been able definitely to identify, such as (1) the effect of the state of water reserve of the tissues, and (2) the chilling of the body surface.

These factors can function significantly to distort the test-meal reaction when viewed in the terms suggested by Mosenthal.

When so functioning they affect chiefly the fluid element in the test-meal reaction complex; and this mainly by virtue of the fact that the skin and lungs make a preferential and significant demand on body fluids, whereas the excretion of solids by the skin and lungs is practically negligible.

These varying extrarenal influences are sufficient to require judgment with reservation as to renal functional efficiency on the basis of the suggested method of test-meal interpretation, especially:

1. On the basis of a single test meal (unless the reaction gives evidence of marked renal insufficiency).

2. In individuals who are well enough to be about and are exposed to the diverse influences of temperature, relative humidity and rate of metabolism.

3. In cases in which no strict control of the dietary of the test meal is attempted.

By reason of these circumstances, early diagnosis, by this method of renal insufficiency, is hazardous unless frequent tests consistently show renal involvement.

Studied as groups, the several classes of kidney nephropathies have presented the various types of pictures described for them by Mosenthal. This last statement we submit as a summary of our findings in over 200 routine test

meals to nephritic patients in the medical ward of Roosevelt Hospital.

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CARCINOMA OF THE COLON*

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THIS report is based on a study of 69 cases of carcinoma of the colon excluding the rectum, treated on the Second Surgical Division of the Roosevelt Hospital since 1909.

The grave character of the disease, the high operative mortality, the frequency of recurrence after resection, the large percentage of cases too advanced to permit of removal when first seen, all tend to make the outlook in these cases far from encouraging.

It is the object of this paper to try to demonstrate the fact that carcinoma of the colon compares favorably with malignant disease elsewhere in percentage of operability and in favorable results both immediate and late, following radical operation.

It is true that many cases first seek surgical advice when the disease is well advanced and beyond hope of surgical cure. Many are first seen in acute obstruction when the diagnosis can only be surmised and emergency colostomy or enterostomy must be resorted to as a life-saving measure. Some of these patients when questioned later give a history of increasing constipation or attacks of partial obstruction, which should have given warning leading to an earlier diagnosis; other attacks come suddenly in patients in apparent good health.

A case now under my care illustrates this type. A woman of fifty had always been well until January of this year, when she had an attack of cramp-like abdominal pain attributed to indiscretion in diet. This passed off under treatment by catharsis in two or three days. There was no previous history of increasing constipation or abdominal pain, and after the attack the bowels moved normally until a

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second attack of pain and distention, occurring three weeks later, failed to respond to catharsis and enemata and on February 6, 1924, emergency cecostomy had to be performed for complete obstruction. Radical operation by the two-stage (Mikulicz) method, performed on March 8th, revealed a large carcinoma at the splenic flexure, without glandular metastases or secondary deposits; the lumen of the gut at the growth was barely the size of a lead pencil. She made a good operative recovery.

The first symptom to attract attention may be attacks of colicky pain with abdominal distention, with increasing constipation in the intervals.

Careful palpation when the abdomen is flat may reveal a mass, especially when it is located in the cecum, ascending or transverse colon, the lower end of the descending colon or sigmoid. When at or near the hepatic or splenic flexures it may be difficult or impossible to locate, as it is also in obese or very muscular patients, or in the presence of abdominal distention.

The discovery of a mass or tumor may be made before any obstructive symptoms have developed or other evidence of disease has appeared; or bleeding from the bowel may be the first warning. Bleeding may appear as a single large hemorrhage, as bleeding repeated in moderate amount or as occult blood in the stools.

In some cases, especially right-colon growths, severe secondary anemia, debility and loss of weight may precede local evidence of the disease.

Whatever the initial symptoms may be, a thorough diagnostic investigation should be made at once and the site of the growth located as nearly as possible.

When advanced obstruction is present, colostomy or enterostomy must precede this investigation, and it is often impossible or unwise to attempt to locate the growth by exploration when this is done. It is far better to do a cecostomy or ileostomy on the right side than to jeopardize the patient by a difficult exploration in the presence of extreme distention.

When the distention is relieved, the abdomen should be carefully palpated for a mass; digital examination of the

rectum (a procedure too often omitted) and sigmoidoscopy should be done; and *x*-ray examination after barium enema, the most valuable of our newer diagnostic methods.

Great care must be taken in interpreting colon roentgenograms, as apparent filling defects occur from various causes and erroneous conclusions are not infrequent. Differential diagnosis must be made from many other conditions which cause obstruction or abdominal distention.

Obstruction from bands or kinks; from partial volvulus of redundant loops of sigmoid; from impacted feces in elderly people; distention from paralytic ileus in the course of systemic disease, e. g., pneumonia, are all conditions in which we have seen errors of diagnosis made.

When the diagnosis has been established and the site of the growth located, either by diagnostic examination or exploratory operation, the plan of treatment must be determined.

In many cases the presence of a large, fixed growth, of local extensions or involved lymph-nodes, or of palpable nodules in the liver, make it all too evident that palliative colostomy is the only operation to be considered.

In the massive advanced growths without much obstruction it is often wise to omit even this procedure, to avoid the distress and annoyance of a fecal opening during the last few weeks of life.

Sometimes a short-circuit operation may be done for obstruction; or it may be justifiable to resect a large painful growth even when nodules are present in the liver, especially when it can be done safely by the two-stage method, for the relief of pain and obstruction.

We have done this twice; once in a recent case still under treatment—a large growth at the splenic flexure, without lymph-node involvement or local extension, but with multiple nodules in both lobes of the liver. The other case, a descending colon growth with liver involvement, recovered from the operation and was relieved of abdominal symptoms but died seventy-three days later of cerebral metastases.

PATHOLOGIC TYPES

There are several gross pathologic types, of which the most common are the round ulcer and the scirrhous contracting growths.

The *round ulcer* gradually increases in size until, if left alone, it finally encircles the gut, contracting as it grows and producing, as a rule, marked constriction. The growth advances in the submucous layer beyond the limits of the ulcer, the edges are piled up and thickened, not generally undermined, the base is covered with unhealthy granulations which bleed easily.

The cases vary in the proportions of cell mass to fibrous tissue, some being quite dense and hard, others spongy and cellular; the latter bleed most easily. While the rate of growth varies greatly, it is often slow, and glandular metastases and the development of secondary deposits in the liver are fortunately often long delayed. It is the type which in the long run offers the best hope of successful eradication.

The *scirrhous contracting type* is also slow of growth, narrowing the gut lumen as the growth progresses until finally attacks of partial obstruction give warning of its presence; or the narrowed opening may be suddenly plugged with a mass of hardened fecal matter, and complete obstruction ensue apparently out of a clear sky. While this type is also of relatively low malignancy with late metastases, not infrequently exceptions to this rule occur in the form of liver nodules, or rectoperitoneal gland involvement.

The gut above the constriction may be much dilated, and its wall thinned. Rupture above the constriction is possible and we have seen it occur in the cecum in one of our cases, the result being a huge intraperitoneal fecal abscess and a fatal issue. In another case, a contracting growth in the middle of the transverse colon in which the obstruction had been relieved by an enterostomy in the small intestine, there was absolute water-tight closure of the lumen of the colon at the time of its resection. Block resection of the colon with end-to-end suture was followed by spontaneous closure of the fecal opening. Death occurred however, within a year, due to extensive metastases in liver and peritoneum.

When constrictions occur in the ascending colon or cecum, the lower ileum undergoes hypertrophy and marked dilatation. This often produces the symptom called stiffening of the bowel, or disappearing tumor. The lower ileum goes into a state of tonic contraction similar to that of the gravid uterus; a tense mass formed by the intestinal coils can be seen and felt, and if the hand is kept on the abdomen, in a few moments the spasm relaxes, the gut wall softens and the tumor disappears. This is simply a later phase of the visible peristalsis seen in these cases.

Perforation of the growth itself from deep ulceration with pericolic abscess formation occurred in 5 of our cases: in 1 the perforation was plugged with an orange seed.

Drainage was done in 2 cases, a cecal growth in a woman of seventy-two, and a descending colon growth in a man of forty-four. Simple drainage of the abscess was followed by a fatal result in the cecal case in twenty-four hours; drainage of the abscess and cecostomy by death on the sixth day in the second case.

A third case made an operative recovery after drainage of the abscess with a short-circuit operation.

Two cases died promptly of acute sepsis after radical resection, with contamination of the operative field from the perforation—both left colon cases.

A third type is the *massive medullary growth*, with early lymph-node involvement and metastases. These cases grow more rapidly and are prone to hemorrhage.

While attempts at radical resection are usually discouraging in this type, one of our cases, a man twenty-nine years of age, the youngest of the series, lived for three years and four months after operation, an extensive right colon resection, and had more than two years of active work in comfort, as principal of a large public school. The growth was of the medullary type with colloid formation; lymph-node involvement was quite extensive at the time of operation.

We have had 67 cases of carcinoma of the colon on the Second Surgical Division of The Roosevelt Hospital since 1909.

Of these, 37, or 55 per cent, have been treated by radical resection: 19 right-colon growths and 18 left-colon.

Of the right-colon growths, 17 were resected by one-stage method with immediate suture: 13 side-to-side; 3 end-to-end; 1 end-to-side. Of the 17 cases, 15 recovered. Two died—one recent case end-to-side suture from obstruction at the site of anastomosis, died in spite of a secondary enterostomy; the other, after the wound had healed and he was out of bed, on the thirty-third day after operation died from cardiac decompensation. The operative mortality of this group was 11.7 per cent, or excluding the cardiac death, 5.8 per cent.

Two right-colon cases were resected by the two-stage method: 1 recovered and 1 died.

Of the 18 left-colon resections, 8 were done by one-stage resection with immediate suture, with 3 deaths, all due to acute sepsis, a mortality of 37.5 per cent.

Ten were done by the two-stage method with 3 deaths, a mortality of 30 per cent. Of these, 2 were due to acute sepsis and 1 to late cerebral metastases. The operative mortality of the series of 37 cases with 9 deaths was 24.3 per cent.

A study of these statistics illustrates the fact that resection of the left colon is attended by a higher mortality than resection of the right colon, in which a one-stage operation with immediate suture is a relatively safe procedure; that the difference is due to the higher infection potency of the left-colon content (a fact long recognized) and also to the greater difficulty of securing healing without leakage in suture of the left colon.

These facts are leading us more and more to resort to the two-stage procedure of Mikulicz in left-colon growths, and we believe that this procedure will greatly reduce the mortality in this group in spite of the fact that the results in the short series quoted do not demonstrate this. The real operative mortality in the 10 cases so treated, excluding the late death (seventy-third day) from cerebral metastasis, was 20 rather than 30 per cent, while the mortality, all due to acute sepsis, of the one-stage method was 37.5 per cent.

Three of our right-colon cases had severe secondary anemia when first seen, with the following blood counts:

Hemoglobin.....	35 per cent	R.B.C.....	2,914,000
Hemoglobin.....	40 per cent	R.B.C.....	3,368,000
Hemoglobin.....	46 per cent	R.B.C.....	4,000,000

All were transfused first, and a one-stage enterocolectomy performed, by lateral suture. All made excellent recoveries and are now well at thirteen years, nine years, and three years and ten months respectively.

Right-colon growths, even without gross hemorrhage, are prone to produce advanced degrees of secondary anemia, with great debility, the exact cause of which is somewhat obscure. They offer, in spite of this, some of the best prospects for a radical cure, as several cases in our series illustrate.

We quite appreciate that the above results are not brilliant; and we must turn to late results for a more hopeful view of the prognosis.

Of the 28 cases which recovered from radical resections, 15 are alive and well at the present time without recurrence; 1 is alive with recurrence at four years and four months after operation. One was well six and a half years and then lost to our follow-up in 1916; one died eight years after operation, free from recurrence following an operation for septic cholangitis; one two and a half years postoperative free from recurrence, following an extensive resection for persistent colostomy opening—a remarkable and complicated case to which I will refer later.

Out of 28 cases therefore, 17, or 60.7 per cent, are well or died free from recurrence after long periods. One lived six and a half years and was lost track of, raising the per cent to 64. One is well four years and four months with recurrence.

Of the other late deaths, 1 followed 6 months after a second radical resection for local recurrence at the ileocolic junction, five years after the first operation. One was well eighteen months, developed recurrence and died three years and two months after the primary operation. Seven died of recurrent disease at from eight to eighteen months after operation.

The cases now alive and well are at the following periods after operation: fifteen years—1; thirteen years—2; nine years—1; four years—3; two and one-half to three years—2; one year, ten months—1; one year, five months—1; seven months—1; less than four months—3.

It is the study of these late results which gives the grain of comfort in the study of cancers of the colon: results which compare very favorably with the results of cancer removal in other parts of the body.

Some of the individual cases present features worthy of mention: A man seventy-five years of age, with a large carcinoma at the splenic flexure and commencing obstruction, was resected by the two-stage Mikulicz method, made a good recovery and is now well and free from recurrence at one year and ten months postoperative. He spent all last summer traveling in Europe. Nineteen years before operation a carcinoma of the sigmoid had been resected successfully by another surgeon, and the sigmoid and lower descending colon were entirely free from recurrent growth.

A woman of sixty-five years was operated upon for a transverse-colon growth quite adherent posteriorly to a retroperitoneal mass of glands, and thought to be inoperable. A short-circuit operation was done between the transverse colon distal to the tumor and the ascending colon. Leakage occurred and a wide-open fecal fistula developed. After a period of three weeks in which death was expected at any hour, she began to improve; later an evaginated protrusion of gut, bearing at its apex a round-ulcer type of carcinoma, appeared in the fistula and finally protruded so far that the growth, with a good length of telescoped gut, was cut off, and the ends sutured together. Recovery followed, but the fecal opening persisted, and two and one-half years later, after insistent demands on the part of the patient, extensive resection was done for cure of the fistula, followed by death from peritonitis on the sixth day. There was no recurrence of the disease. The retroperitoneal invasion noted at the primary operation was evidently an inflammatory mass. This instructive and disappointing case illustrates the well-known fact that adjacent infiltration and gland involvement associated with ulcerated growths may be inflammatory and not malignant.

SUMMARY

1. Cancer of the colon excluding the rectum offers a relatively high rate of operability and a percentage of

radical cures which compares favorably with that of malignant disease in other organs.

2. Growths of the cecum and right colon, including the right part of the transverse colon, are suitable for a one-stage resection with immediate anastomosis by suture. The operative mortality should be relatively low.

3. Left-colon growths are more safely resected by the two-stage Mikulicz method.

CHRONIC DUODENAL AND GASTRIC ULCER*

THE PRESENT STATUS OF SURGICAL TREATMENT

CHARLES H. PECK, M.D.

THE surgical treatment of chronic duodenal and gastric ulcer is still a matter of controversy both as to operative indications and the best type of procedure. As the two groups present radical differences in pathology, prognosis and surgical management, it is well to consider them separately. Acute perforations will not be considered in this paper, as the problems involved are quite distinct and demand special consideration.

CHRONIC DUODENAL ULCER

As to indications for surgical treatment in this group, most surgeons differ less from the medical viewpoint than is popularly supposed. They are quite content to let the internist treat these cases as long as physician and patient are satisfied that treatment gives relief and a cure is being effected.

We agree with the internist that early uncomplicated cases should first receive medical treatment; and that a considerable number of patients are cured or at least kept in reasonable comfort thereby for long periods of time. It is a well-recognized fact that many patients prefer to bear recurrent periods of discomfort, rather than submit to the hazards of an operation, and are willing to accept a certain percentage of risk as to the possible occurrence of hemorrhage, perforation or obstruction.

The surgeon has no quarrel with such patients, provided they have a clear understanding of the situation. Ample opportunity for surgery exists in patients who fail to respond

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properly to medical treatment, in those unwilling to endure repeated relapses, and in cases in which complications threaten or occur.

We prefer that patients should have had a thorough and intelligent trial of medical treatment before surgery is considered, and have repeatedly expressed this view to patients with early symptoms of short duration, a fair number of whom never come to operation. I would emphasize especially those in whom a hasty or ill-founded diagnosis has been made, unsupported by adequate clinical symptoms. While I wish in no way to disparage positive *x*-ray evidence of ulcer so often valuable and unmistakable, I do feel that the greatest care should be taken in the interpretation of short series of doubtful plates. Cole's insistence on the need of a sufficient number of plates for safe interpretation has been a great advance in this particular diagnostic field.

The roentgen diagnosis of adhesions about the duodenum and gall-bladder, giving the impression that ulcer or some surgical lesion may be present, without venturing a positive opinion, must also be taken with caution, as we have seen many negative explorations in such cases.

To return to the management of uncomplicated chronic duodenal ulcer which has resisted medical treatment, in which the diagnosis after careful study seems reasonably certain, and in which the need for surgery of some sort is conceded:

We have been considerably disturbed by the tenor of several papers and discussions, and the attitude of a number of prominent surgeons as expressed at recent important meetings, notably in the New York Surgical Society during the past year; at the Clinical Congress of Surgeons held in Chicago in October, 1923, and at the last meeting of the Southern Surgical Association.

The attitude which disturbed us was the tendency to advocate radical measures of resection, often of large portions of the healthy stomach, for the surgical cure of this disease.

We cannot subscribe to the recent wave of enthusiasm for these radical methods, which seems to be gaining so many advocates.

A distinguished foreign surgeon has recently been demonstrating partial gastrectomy under local anesthesia for this type of case, removing a considerable portion of the healthy stomach for the purpose of getting rid of small uncomplicated duodenal ulcers. One of the arguments advanced in support of the procedure is that it lessens or removes the danger of the subsequent development of gastrojejunal ulcer, which occurs in about 2 per cent of cases following gastroenterostomy.

Van Haberer of Innsbruch advocates extensive resection followed by gastroduodenal anastomosis—a modification of the Billroth 1. method of gastric resection—and has numerous admirers and imitators in this country.

One of the soundest and safest of our American surgeons has recently brought forward a method of excision in which the cut end of the stomach is anastomosed to the side of the mobilized duodenum, the cut end of which has been closed by a purse-string suture, i. e., a new type of pylorectomy.

He has never liked gastroenterostomy, nor has he practiced it to any extent in his clinic. When he refers to it in discussions it is generally to condemn it and to cite some case in which it has failed to relieve the condition for which it was done.

Our own experience and belief is that simple gastroenterostomy, properly performed, is curative and adequate in the great majority of chronic duodenal ulcers; that from 80 to 90 per cent of the patients so treated are completely relieved of their symptoms and remain well as they are followed year after year; that the operation is as successful in the average case without obstruction as in those with it; that malignancy develops so rarely as to be a negligible factor in prognosis.

We do not believe in, nor have we practiced, any method of pyloric exclusion; our experience with this procedure therefore is nil. We have yet to see reported any series of cases which would support the claims made by the advocates of this procedure. The viewpoint of surgeons who believe in this method whom we have heard discuss the question has been quite theoretical and unsupported by any considerable amount of experience.

We have certain theories as to why gastroenterostomy so often effects a cure in chronic duodenal ulcer, and we believe that mechanical and chemical factors in its etiology have a distinct bearing on the results.

The ulcers nearly all develop within 1½ inches of the pylorus, the part of the duodenal wall subjected to the impact of spurts of acrid stomach content, pumped intermittently through the pylorus as though by the piston of a powerful syringe. This stomach content is often equivalent to a strongly irritant or even corrosive chemical compound, not entirely dependent on the amount of hydrochloric acid present for its irritant character.

When we think of the combinations of food and drink with which most of us from time to time insult our gastrointestinal tracts, it is not surprising that by the time the mass is pumped in spurts through the pylorus, it is acrid enough to burn a hole in shoe leather, to say nothing of the delicate duodenal mucous membrane.

When the ulcer is once formed, as Codman well says, it may be likened to a fissure in ano; an ulcer within the grip or influence of a constantly moving sphincter, irritated by the impact of acrid stomach content, with little chance to heal and every chance to become deeper and develop a zone of chronically irritated and inflamed tissue around it.

Gastroenterostomy modifies both chemical and mechanical influences:

1. It lessens the irritant character of the stomach content, partly by shortening the length of time in which it is churned about in the stomach; partly by actual diminution of the acidity.

2. It greatly lessens the amount of stomach content still passing through the pylorus, even when there is no obstruction, and also the force of impact on the ulcer area of that which does pass.

Whatever the real explanation may be, we have abundant clinical evidence that duodenal ulcers heal after gastroenterostomy; that they remain healed and that patients are permanently cured by their symptoms in a large percentage of cases so treated.

We do not believe that gastroenterostomy should go into the discard in the treatment of duodenal ulcer, nor do we believe that extensive resections of normal stomach are justifiable for this lesion.

We are still unconvinced that resection to prevent the formation of gastrojejunal ulcer is a proper procedure in the 98 cases that do not need it to avoid possibly its occurrence in the other 2. The other 2 might well be dead before the hundredth case is reached, if this were made a routine operation.

Moreover, we believe that with a well-planned and uniformly executed technique for gastroenterostomy, even the 2 per cent of gastrojejunal ulcers may perhaps be reduced to a lower figure.

The choice of procedure is a problem of prime importance and depends to some extent upon the pathologic type of the ulcer. For a better understanding of this it is well to group the cases into general types. Leaving out acute perforations which constitute a special problem, four such groups will be sufficient for our purposes:

1. Small, single, anterior wall ulcers, without narrowing of the gut, susceptible of local excision, without encroaching to any extent on the duodenal lumen or pylorus. As recently pointed out by Judd and Rankin, local excision without gastroenterostomy is quite sufficient in this type; but the percentage of ulcers suitable for this procedure is limited.

2. Chronic indurated ulcers without obstruction; single or multiple. We include in this group ulcers of the chronic perforating type; with adhesion fixation of the duodenum or inflammatory mass. A majority of all duodenal ulcers fall in this class.

We have had many cases of chronic perforating ulcers without hemorrhage, but with extensive adhesions, fixation of the duodenum, sometimes a considerable inflammatory mass. In many of these cases radical resection would be difficult, hazardous or quite impossible. If resorted to at all in this type it is well to do a gastroenterostomy first, following by resection as a two-stage procedure ten to fourteen days later. The inflammatory mass may be found greatly

diminished in size, fixation less marked, and radical excision much easier and less dangerous.

We believe, however, that gastroenterostomy alone will cure a large percentage of these cases, and that more radical methods are generally unnecessary and unwarranted.

3. Cases with duodenal stricture or so-called pyloric stenosis, a group in which gastroenterostomy is the ideal operation, and in which there is the least controversy as to its efficiency. In no field of major surgery are the results of a relatively simple operation more brilliant and lasting.

We have repeatedly operated upon cases with strictures so tight, and starvation and dehydration so extreme, that the condition at the time of operation was most critical.

Preliminary hypodermoclysis, blood transfusion and operation under local anesthesia often aid in obtaining a successful outcome.

4. Cases in which severe hemorrhage has occurred, single or repeated. Hemorrhage occurs most frequently in deep penetrating ulcers on the posterior wall or against the head of the pancreas; often also in multiple ulcers.

We have seen patients die of duodenal hemorrhage before any operation could be performed; cases so exsanguinated that preliminary blood transfusion alone made operation possible.

Gastroenterostomy is not a guarantee against recurrence of hemorrhage which may prove fatal. If the patient's condition permits, excision of the ulcer area is desirable in this group. If the danger of radical excision seems too great in exsanguinated or debilitated cases, gastroenterostomy may be sufficient, or it may be done as the first step of a two-stage operation.

It is our belief that the average duodenal ulcer heals within two to four weeks after gastroenterostomy; but fresh hemorrhage may occur before time for such healing has elapsed.

Repeated blood transfusion in moderate amounts (300 to 500 c.c.) is especially valuable in these cases. We have had several hemorrhage cases in which gastroenterostomy has effected a cure without return of the bleeding; and a few cases in which we have performed immediate pylorectomy.

We were once reluctantly forced to operate on a woman seventy-four years of age for repeated duodenal hemorrhage extending over a period of fifteen months. Simple gastroenterostomy was done, there was no recurrence of hemorrhage, and she was alive and well, eating heartily, without symptoms, at the age of eighty. We have found that hemorrhage, either from stomach or bowel or both, occurred in about 14 per cent of our cases.

We believe that radical resections should be reserved for the small percentage of cases in which gastroenterostomy has failed to relieve the ulcer syndrome; for certain hemorrhage cases; cases of inflammatory mass in which malignancy may be suspected (a two-stage procedure); and possibly for the 2 per cent in which gastrojejunal ulcer develops.

If gastroenterostomy is to be successful and free from complications, it is essential that a well-thought-out, routine technique should be employed. In perhaps no operation are slight errors in detail more fraught with danger of subsequent trouble.

We are quite aware that our own method is not the only good one, but in our experience it has proved satisfactory and free from early or late complications.

We believe that every surgeon should carefully work out the details of the routine which in his hands gives a uniformly smooth postoperative course. We have had in our series, only 2 cases of vicious circle, both occurring in cases in which the gastroenterostomy had to be done through an incision planned for other work owing to an error in preoperative diagnosis. Both cases recovered after secondary entero-enterostomy and are now well and free from symptoms at seven years, ten months, and three years, ten months, respectively.

OPERATIVE TECHNIQUE

There are several points in technique which we believe to be of importance in the operative procedure.

Our own routine is to stand on the patient's left, and make a left paramedian incision. This falls directly over the site where the stoma is to be made, and where the duodeno-jejunal junction lies.

The stoma is placed at the most dependent part of the greater curvature, in a line directly below the cardiac orifice.

First the stomach, then the jejunum, are grasped with shallow curved Moynihan stomach clamps. The placing of the clamp on the stomach is important; the line is from greater curvature upward and to the left. Great care must be taken to see that the point nearest the greater curvature corresponds to the distal point on the jejunum. The jejunum is grasped about 3 inches from the duodeno-jejunal junction.

The clamps are locked; all viscera, except the portion in the grasp of the clamps, are replaced within the abdomen; and hot towels protect the wound beneath the clamps.

A simple whip-over suture of linen is used for the outer tier, the posterior half of which first joins stomach and bowel wall for a length of 2½ inches. Openings 1¾ inches long are then made in stomach and jejunum, escaping content being carefully caught on sponges.

No individual vessels are caught and the mucous membrane of both stomach and bowel is purposely left redundant. This insures perfect covering of the cut edges of stomach and duodenal walls, leaves no cracks into which gastric juice can seep, and is an important factor in the prevention of subsequent gastrojejunal ulcer. The posterior half of the inner tier is then made with special tanned catgut, a simple continuous whip-over stitch, great care being taken to see that every stitch includes all layers of stomach and gut walls; that spacing is accurate and tension constantly maintained, just enough for firm contact without blanching the tissues. Postoperative hemorrhage cannot occur if this suture is properly placed.

A double half-hitch to lock the suture is taken at the turn, and the same whip-over stitch is continued back completing the anterior half of the inner tier. Separate thrusts of the needle through each edge are necessary on this return stitch, and the same extreme care is taken with spacing, tension and mucous membrane edge approximation. The tie is made to the end of the same suture left long at the start. The anterior half of the linen outer tier stitch is then completed.

The stoma almost uniformly measures 1¾ inches in the clear and the outer line of suture 2½ inches.

The clamps are removed, and the low point of the edge of the opening in the transverse mesocolon, (i. e., the point nearest the wall of the colon) is attached to the stomach wall at the distal end of the stoma, with interrupted fine catgut. Similar sutures complete the attachment of the edges of the mesocolic opening to the stomach. This step is important as it prevents herniation of the gut, allows the mesocolon to cover and protect the suture line, and maintains proper position of the stoma, which now lies vertically, the jejunum pointing directly downward, and swinging easily from side to side.

The belief that the stoma frequently contracts after gastroenterostomy in cases in which the pylorus remains patent has long been disproved by *x*-ray studies made, in many cases, years after the operation. We believe that a painstaking technique with careful apposition of the cut edges of the mucous membrane which prevents open cracks in the suture line left to heal by granulation, does much to guard against the later formation of a contracting cicatricial ring.

We have had 194 cases of chronic duodenal ulcer—74 reported in 1915, and 120 since that time. We have had no case of postoperative hemorrhage in the series, a fact which adds to our feeling of confidence that the method of suture employed ensures complete hemostasis.

We believe that in the various types of running mattress stitch, vessels may be "jumped" and left to bleed, in occasional instances.

As far as we know, there have been only 2 proved cases of marginal ulcer, and 1 suspected, which did not come to secondary operation and later became symptom-free. We repeat our belief that painstaking apposition of redundant mucous membrane edges safeguard appreciably against this condition.

SUMMARY

1. Surgical treatment of duodenal ulcer should not be resorted to until it is evident that the case is chronic and

that medical treatment has failed to give adequate relief or to effect a cure.

2. The operation of choice should be simple gastroenterostomy without pyloric exclusion. The more radical methods of resection should be reserved for cases with severe hemorrhage, those in which the simpler operations have failed to give relief, or cases of gastrojejunal ulcer.

Gastric ulcers, or cases in which the ulcer has invaded and passed the pylorus into the stomach wall, are not considered in this summary.

3. A lasting clinical cure may be expected in at least 80 to 90 per cent of cases treated by simple gastroenterostomy.

CASE REPORTS

W. K. K. Posterior gastroenterostomy May 13, 1916.
Chronic duodenal ulcer with stenosis.
Well Feb. 27, 1924.

W. W. Posterior gastroenterostomy June 3, 1916.
Indurated interior duodenal ulcer $\frac{1}{2}$ inch from pylorus without obstruction.
Well Feb. 27, 1924.

W. M. M. Posterior gastroenterostomy April 22, 1916.
Indurated duodenal ulcer with adhesions, $\frac{3}{4}$ inch from pylorus; anterior; no stenosis.
Vicious circle—persistent vomiting.
Secondary enteroenterostomy, May 6, 1916, by Murphy button. Slow convalescence but good recovery.
Intestinal hemorrhage, January, 1922. No recurrence since that time.
Free from symptoms Feb. 27, 1924.

F. W. S. Posterior gastroenterostomy May 10, 1919.
Chronic duodenal ulcer—anterior; $\frac{1}{2}$ inch from pylorus; duodenum fixed by adhesions; no obstruction.
Symptoms dating back many years.
Operation for appendicitis with abscess, Sept. 8, 1915.
Symptom-free since gastroenterostomy—now five years postop.

J. D. B. Posterior gastroenterostomy Oct. 24, 1916.
Chronic indurated duodenal ulcer without stenosis.
Duration of symptoms prior to operation, seven years.
Complete relief of symptoms.
Well now eight years postop.

A. C. H. Posterior gastroenterostomy Dec. 16, 1922.
Chronic duodenal ulcer with extreme stenosis, complete occlusion probable for several days prior to operation. Extreme starvation and dehydration.
Total duration of symptoms, five or six years.

Preoperative transfusion.
Good recovery.
Symptom-free since operation.

J. A. M. Posterior gastroenterostomy Jan. 8, 1916.
Chronic perforated duodenal ulcer with inflammatory mass.
Three previous periods of illness suggestive of sealed perforation of ulcer during the past year.
Symptom-free since operation.

TUBERCULOUS CYST OF THE SPLEEN: SPLENECTOMY; RECOVERY*

CHARLES H. PECK, M.D.

PRIMARY tuberculosis of the spleen is a condition uncommon enough to warrant recording as cases are observed. We have recently, at The Roosevelt Hospital, operated upon such a case, which presented some unusual features, notably the size of the spleen, the extent of destruction of splenic tissue with the capsule still intact and the very mild degree of constitutional reaction.

In classifying the case as primary tuberculosis of the spleen, we mean simply that there was no clinical evidence of other tuberculous lesions which might have assumed the rôle of a primary focus, except tuberculous lymph-nodes of moderate size and chronic type, though we are, of course, unable to state definitely that no such focus existed.

The patient was a native of Antigua, B. W. I., colored, aged twenty-six years, married, laborer. He had lived in the United States since 1920. He was admitted to The Roosevelt Hospital on November 15, 1922, to the medical service, Dr. Evan Evans, attending physician. The condition which brought him to the hospital was not the splenic condition, but a loss of sexual power, for which he sought treatment.

History. A gradual enlargement of the abdomen had been noticed for about four months. He had no real pain, but had recently begun to have discomfort over the left upper abdomen and lumbar region. Exacerbations of moderate pain in this region occurred in April and October, 1922. He had recently had some shortness of breath on exertion, and occasional slight cough; he was subject to "colds." He was said to have had yaws when eight years old; Neisser infection five years ago; questionable chancre six years ago. No history of chronic illness.

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Physical Examination. This showed good general physique and nourishment. Cardiac and pulmonary signs normal; slight enlargement of cervical, axillary, epitrochlear and inguinal lymph-nodes; no periosteal nodes; reflexes normal; eyes normal. A large mass filled the left upper abdomen; it extended 2 cm. beyond the midline to the right; downward to the level of the iliac crests; it had the general position and

FIG. 39. Tuberculous cyst of spleen. Dimensions: 29 by 18.5 by 15 centimeters. Diameter of large cyst 11 centimeters. Weight, 3,270 grams.

shape of the spleen; its surface was smooth, edges hard and rounded; center soft and fluctuating. It moved slightly with respiration; was not tender; the greatest circumference of the abdomen was 84½ cm. The liver edge was felt 3 inches below the costal margin; it seemed normal and was distinct from the mass. There was no evidence of ascites.

Weight, 149½ lbs; blood pressure, $^{103}/_{78}$; hemoglobin, 65 per cent; r.b.c. 4,350,000; w.b.c. 8,000; polynuclears, 85 per cent; eosinophiles, 2 per cent; Wassermann, 4 plus. Blood chemistry, normal; Urine, trace of albumin, a few casts at times, otherwise negative.

Temperature range: Nov. 15, 1922, 99° to 100.8°; later normal most of the time. Pulse and respiration normal.

Antiluetic treatment given (not salvarsan). No diminution in size of spleen; no change in symptoms or signs.

X-ray Examination. This showed descending colon pushed way to the right by mass; otherwise negative. *X*-ray of chest, negative.

Cervical lymph-node, removed for diagnosis, showed chronic tuberculosis.

Operation. He was transferred to the second surgical division on Dec. 7, 1922, and splenectomy was performed on Dec. 9th, through a longitudinal incision at the inner third of the left rectus. The mass proved to be a huge cystic spleen, very adherent to the surrounding structures. The

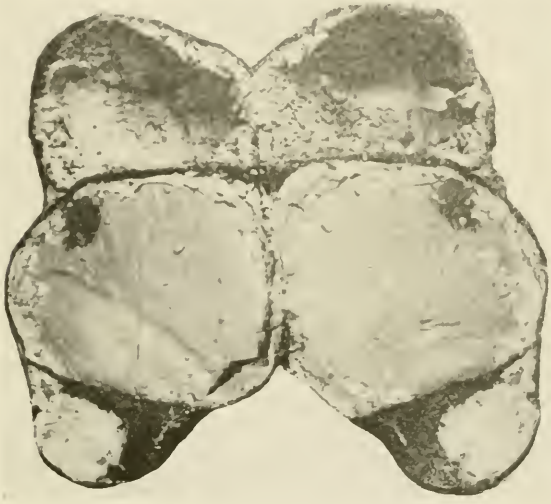

FIG. 40. Spleen bisected and laid open.

lower pole and body of the mass were first freed and delivered; adhesions clamped and ligated as operation proceeded. The upper pole was firmly adherent to the diaphragm and splenic flexure of the colon; the dense adhesions were separated and divided, partly by sharp dissection, and with great difficulty. During the dissection a large *locule* of the cyst at the upper pole ruptured, and curdy, yellowish-white material escaped. The mass was finally freed except at its pedicle and a large gauze pack filled the huge space beneath the diaphragm. The vessels of the pedicle were comparatively small and were secured without difficulty, and the mass removed. After careful hemostasis the wound was closed without drainage. There had been no damage to adjacent viscera and comparatively little loss of blood.

The time of operation was one hour and forty-five minutes; condition poor. An infusion of 700 c.c. of salt solution was given on the table, followed by a transfusion of 448 c.c. of blood on his return to the ward. His condition was critical for the first two or three days, after which the convales-

Fig. 41. Patient nine months after operation.

cence was uneventful. The wound healed *per primam*. The temperature ranged from normal to 102 to 103° for twenty days postoperative, finally remaining normal after the twenty-fourth day. He was discharged on Jan. 3, 1923, twenty-five days after operation.

Gross Specimen. The removed spleen was enormous in size; the lower two-thirds was occupied by a huge cyst locule filled with a jelly-like material; the locule at the upper pole, ruptured in removal, was much smaller; a very little thinned-out splenic tissue remained in the septa

between the locules; hardly any at the periphery. Its dimensions were 29 × 18½ × 15 cm. Its weight was 3270 grams (16 lbs., 13 oz.), after the loss of the semifluid content of the upper locule of the cyst. The large cyst measured 11 cm. in diameter. Only 3 cases of equal or larger size have been recorded, all autopsy and not operative cases.

Microscopic Sections. Sections showed no typical tuberculosis or other characteristic lesion; a probable diagnosis of tuberculosis was made on the gross pathology.

Animal Inoculations. A guinea pig inoculated with contents of cyst on Dec. 9, 1922, autopsied on Jan. 8, 1923 (thirty days), showed general miliary tuberculosis.

Winternitz, in 1912, reported a collected series of 51 cases of primary tuberculosis of the spleen, of which 34 were autopsy findings and only 17 operative. Of the 17 operated upon 10 recovered and 7 died. Royster operated successfully upon a case in January, 1911, and Giffin in 1919 reported a case of successful splenectomy (weight 508 gm.), well two years at the time of the report. He also adds a case of successful splenectomy (weight 625 gm.) for secondary tuberculosis of the spleen, with a healed pulmonary lesion at the right apex, well two years and four months after operation. Giffin also reports 2 interesting autopsy cases, 1 with blood findings simulating pernicious anemia and 1 with leucemia, in both of which the spleen showed extensive tuberculosis.

The careful and thorough review of Winternitz brought out many interesting facts relating to the condition:

The age, by decades, of 45 of the 51 cases in the series was: 1st, 5 cases; 2d, 3 cases; 3d, 12 cases; 4th, 10 cases; 5th, 6 cases; 6th, 2 cases; 7th, 5 cases; 8th, 1 case. Examination of the blood was noted in 26 cases. It was normal in 9, moderate secondary anemia was present in 11, and there was a definite polycythemia in 6, the red cell count ranging up to 8,000,000 or more. The leucocytes were not generally increased.

Other authors have noted the tendency to polycythemia in tuberculosis of the spleen: Douglas reported a marked instance in a man, aged thirty-nine, the red cell count running as high as 8,800,000. Death occurred nine days after splenectomy. Of the 6 cases of polycythemia cited by Winter-

nitz, 4 were autopsy cases; in 1 the result was not stated and 1 (6,000,000 red blood cells) recovered after operation. Splenectomy in the polycythemia of Vaquez's disease is generally fatal, or fails to arrest the disease, and is contraindicated (Moynihan.)

The weight of the spleen in 31 recorded cases was as follows: 8 cases, 150 to 500 gm.; 5 cases, 500 to 1000 gm.; 6 cases, 1000 to 1500 gm.; 7 cases, 1500 to 2000 gm.; 2 cases, 2000 to 3000 gm.; 3 cases, 3000 to 4000 gm. As previously stated the 3 cases of over 3000 gm. were all autopsy cases.

Lymph-nodes examined in 35 cases showed no clinical enlargement in 29 (82.8 per cent). The prominent symptoms in most of the cases were splenic tumor and pain in the splenic region. The course was chronic in a majority of the cases and rapidly progressive in a few.

SUMMARY

Primary tuberculosis of the spleen, though rare, is a distinct entity and is curable by operation in favorable cases. Without splenectomy a fatal termination is inevitable.

Splenectomy is indicated in certain cases of secondary tuberculosis of the spleen, when the splenic lesion is predominant and the supposed primary lesion is a healed tuberculosis or susceptible of cure.

Giffin's case is an example of this condition. Polycythemia occurs in a certain percentage of cases and probably adds to the gravity of the prognosis, but does not contraindicate operation when the splenic tuberculosis is the dominant factor in the case. The prospect of a complete cure and restoration to health in patients surviving splenectomy is demonstrated by several of the reported cases.

ACUTE SUPPURATIVE PLEURISY*

AN ANALYSIS OF NINETY-FOUR CASES

CHARLES H. PECK, M.D., AND
HENRY W. CAVE, M.D.

THIS paper is based upon an analysis of 94 cases of acute suppurative pleurisy, treated upon the surgical services at The Roosevelt Hospital, from Jan. 1, 1915, to Jan. 1, 1920, a period of five years. Only 11 of these were postinfluenzal, the remainder being postpneumonic. In this respect the material in this study differs from that contained in many of the recent, exhaustive, war-time reports.

The condition is usually secondary to pneumonia, either of the pneumococcic or streptococcic type: in adults, most often a lobar pneumonia; in children, frequently a bronchopneumonia. In certain cases it is impossible definitely to demonstrate a pre-existing pneumonia.

Barjon's[1] idea that empyema usually originates in an infection of mediastinal lymph-nodes, with dissemination through the interlobar spaces of the pleural cavity, while an interesting theory, still lacks confirmation as a preeminent etiological factor.

In the bacteriological study of our series, we found the pneumococcus present in 33 of the 94 cases. Grouping was done in only 22 of these cases with the following results:

	Cases
Group I	7
Group II	2
Group III	5
Group IV	8

The streptococcus was isolated in 10 cases, staphylococcus in 5, and mixed infection in 5. Our records are incomplete as to culture in the remainder and in those in which the cul-

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tures proved sterile. In 77 of the cases the exudate was of the classical, thick, purulent variety; in 10 seropurulent; and in 7 the character was not noted.

The exudate of the pneumococcus contains more fibrin, is usually more quickly walled off, and somewhat less abundant than that of the streptococcus, which is prone to produce a thinner generalized exudate of large amount. This fact becomes of great importance in considering the dangers of open, sucking pneumothorax following early operation for empyema of the streptococcic type.

Butler's[2] notation that in civil life the pneumococcus is found twice as frequently as the streptococcus, is borne out by our own experience. He states that these two organisms are the causative factors in 75 per cent of cases in civil practice, whereas in military life approximately 80 per cent of the post-pneumonic cases were due to the streptococcus alone.

Lord[3] in an analysis of 200 cases found the pneumococcus in 39.4 per cent, streptococcus in 20.4 per cent, staphylococcus in 3.6 per cent, mixed infection in 16 per cent, and in 18.2 per cent the cultures were sterile.

Other occasional etiological factors, such as penetrating wounds, chest-wall injuries, suppurative disease of the mediastinum or adjacent viscera, etc., do not appear in this series, with the exception of 3 cases, secondary to lung abscess. In 1 case of pneumococcus empyema, pulmonary tuberculosis had pre-existed for eleven months. The following are some observations brought out in the study of the series: There were 62 males and 32 females. The average age was twenty and four-tenths years. The oldest patient was fifty-two years of age, the youngest, nine months. The average time from the onset of the illness to the day when the diagnosis of empyema was made was thirty-eight and two-tenths days.

69 cases were postpneumonic.
11 cases were postinfluenzal.
3 cases were secondary to lung abscess.
In 11 cases the pre-existing cause was undetermined.
34 cases were on the right side.

52 cases were on the left side.
In 8 cases the location was not noted.
18 were in the upper half of the chest.
70 were in the lower part of the chest.
60 were localized.
17 were general.
5 were interlobar or sacculated.

No case of bilateral empyema was noted in this series.

Roentgenographic studies were made in many of the cases and were often of great value, but were not sufficient in number to be presented in statistical form.

In considering symptoms and signs, a delayed convalescence following pneumonia or influenza, with recrudescence or persistence of fever and signs of sepsis, should always suggest the possible development of empyema. The usual physical signs of fluid, localized or general, confirmed by roentgenography, fluoroscopy or aspiration, should soon establish a positive diagnosis.

Several cases of the localized and sacculated type presented interesting problems in diagnosis and treatment; 2 were high up beneath the left scapula, posteriorly; 2 presented multiple sacculations.

The treatment of empyema by drainage is one of the oldest operations of surgery. Many efforts have been made to simplify this procedure by substituting less radical treatment. A notable example is the formalin-glycerine injection method so strongly advocated by the late J. B. Murphy,[4] which has failed to fulfil its early expectations as a substitute for drainage.

Simple aspiration, repeated, is valuable as a preoperative procedure, to tide over critically ill cases to a period safer for radical operation; and in a small percentage of cases, especially in children, it will effect a permanent cure in itself. We have had no cures in this series by aspiration *per se*, but have employed it as a preliminary to radical operation in several instances with excellent results.

The same may be said of the minor procedures of inserting small cannulae or tubes through trocar wounds in the intercostal spaces, which we have also done a few times.

These less radical procedures are especially valuable in generalized empyema of the streptococcic or postinfluenzal types, in the early stages when constitutional symptoms are severe and the margin of safety is narrow. They are also useful in severe early cases of the pneumonic type, during the period when radical operation is perilous. An illustrative case was one of pre-existing cardiac disease with marked decompensation and great dyspneic distress, which was temporarily drained by trocar puncture and a small intercostal tube, until improvement warranted radical drainage, eight days later, with ultimate cure. We have employed irrigations with Dakin's solution in a few such cases to prevent clogging of the small tube and facilitate drainage. This method, originated by Mozingo,[5] which we have found so useful as a temporary procedure, we have not succeeded in carrying through to a complete cure of the condition, but have not, perhaps, persisted long enough in the effort to give it a thorough trial. Neither have we used Dakin's irrigations through the small tubes, with the idea of effecting complete sterilization of the cavity in acute cases; though we have used it for this purpose in three instances, in later stages after thoracotomy and drainage.

Some newer methods worthy of mention, with which we have had no personal experience, are the "tidal irrigation" of Taylor[6] of Toronto; the negative pressure closed method of Brix;[7] the oblique intercostal incision with valve-flap action, etc.

Open intercostal tube drainage without rib resection was employed in 15 cases, with 5 deaths, this group representing critically ill cases unsuitable for more radical operation. Local anesthesia was used in 14 of these cases.

Instead of using an incision parallel to the ribs, Morison[9] has suggested a vertical incision down to the ribs and across the intercostal space, with the idea of preventing kinking of the tube by respiratory movement and change of position.

Rib resection was employed in 79 of our series, in the majority of cases using the eighth rib in the posterior axillary line.

In the earlier cases of the series the Brewer spool with siphon bottles or the Connell suction apparatus was the method of choice. Later, on the second surgical division,

the following procedure was adopted as a routine: A large firm rubber tube, $\frac{3}{4}$ in. in diameter and about 6 to 8 in. long, projecting 1 to 2 in. into the pleural cavity, is anchored in position by suture. Gauze plugs on either side and careful suture of the wound angles tend to prevent sucking of air around the tube. The end of the tube is immediately clamped; a small split compress around the tube is at once strapped tightly to the chest wall with adhesive plaster carefully fitted, to complete the air-tight joint. A flange of rubber dam through which the tube passes may be used beneath the strapping to effect a more perfect closure. Gauze pads held by a binder complete the dressing. On return to the ward a long tube of smaller caliber, with its end submerged in solution in a large bottle on the floor at the side of the bed is attached to the large drainage tube by a tapered glass connection. Each inspiration tends to draw a column of fluid up in the tube producing a degree of negative pressure in the pleural cavity. Assuming that an air-tight joint has been secured, no air can enter the chest through or around the tube. Pus from the cavity flows into the bottle and settles at the bottom. Change of the fluid once or twice a day is sufficient, the tube being clamped each time. The amount of pus diminishes rapidly from day to day, and as a rule there is little or no soiling of the gauze dressing on the chest wall. We have repeatedly found it unnecessary to change it for a full week. Offensive pus-soaked dressings are practically eliminated by this method. If the attempt to secure an air-tight joint has failed, complete change of the dressing down to the chest wall and readjustment of the strapping will usually overcome the difficulty.

After the fourth or fifth day the patient is put on Wolff blow bottles, and encouraged to use deep breathing to expand the lung. At from seven to ten days the air-tight drainage has usually accomplished its purpose, the pleural adhesion to the chest wall has progressed to a point eliminating danger of lung collapse. The original tube is removed and replaced by one smaller, but still of good size; e. g., $\frac{1}{2}$ in. diameter, which is cut short and covered by fluff gauze. Within the next week the cavity has as a rule become a simple tube

tract. Tubes progressively shorter and of smaller caliber are used until the tract is simply a thoracic wall sinus.

Throughout the treatment care must be taken to prevent unrecognized plugging of the tube or the formation of lateral pockets. In the later convalescence, balcony treatment, deep breathing and chest and arm exercises are insisted upon.

We have not employed the method of open drainage with Dakin irrigation of the cavity, so widely used during the war, sufficiently to express an opinion as to its value, but feel that the method described has given quite as satisfactory results, both as to percentage of recoveries and time of convalescence.

We have used local novocaine analgesia in 54 cases and consider this the method of choice, especially in critically ill cases. General anesthesia, open drop ether, was employed 35 times, sometimes combined with local, to minimize the amount required. In children general anesthesia is usually necessary.

We cannot claim a mortality to compare with the 4.3 per cent of the Empyema Commission,[8] but have not attempted to exclude deaths really due to the pre-existent pneumonia.

Eighteen of the 94 cases died in the hospital, a mortality of 19.1 per cent. Three deaths attributed to operative shock may well have been due to the existing pneumonia. Two died of pneumonia of the opposite lung, two of cerebral embolism. In 9, death was attributed to sepsis and exhaustion, pneumonia probably being an important factor in some of this group. In 2 cases the cause of death was not stated.

Hemorrhage from intercostal vessels did not occur in this series, but in a recent case, an elderly debilitated patient, death occurred from this cause, nine days after operation, after removal of the drainage tube.

Of the remaining 76 cases, late results are known in 60 (76.3 per cent). Forty-nine cases healed completely, and have remained closed, the average time being nine and one-tenth weeks.

In 11 cases, secondary abscess required opening. One of these has been operated upon three times and still has a

discharging sinus. Two of the secondary operations were done elsewhere.

Another case, operated upon July 1, 1917, developed a secondary abscess in February, 1921, and still has an unhealed sinus. Another case broke open fourteen months after primary closure, final healing being complete in eight months. Eight cases reported secondary operations, 3 of which healed within one year, 5 within two months, after the secondary operation.

SUMMARY

Total cases treated	94
Mortality (18 cases)	19.1 per cent
Closed and remained closed	49 cases of the 60
(average time 9.1 weeks)	(80.1 per cent)
	(late reports)
Persistent sinuses and secondary operations	11 cases

No attempt has been made in this paper to deal with the special problems arising in the management of chronic, late, or neglected cases of empyema, as these form a distinct group in themselves.

CONCLUSIONS

1. The successful treatment of acute empyema is still based upon measures which provide adequate drainage.

2. The principle of air-tight drainage, avoiding an open, sucking pneumothorax, with moderate negative pressure to keep the cavity constantly empty, is of primary importance, and favors the rapid diminution of the size of the cavity until it becomes a simple tube tract. It is one of the greatest recent improvements in the management of these cases.

3. Palliative preoperative measures, e. g., repeated tapping, are important in the early stage of severe cases, especially those of the postinfluenzal or streptococcic types, or when pneumonia is not completely resolved, radical operation being postponed pending improvement in the general condition.

4. Closed tube drainage by the method described compares favorably in results as to recovery and time of healing, with the method of immediately Dakinizing the cavity for

the purpose of sterilizing it. Early bacteriological examination is of aid in determining the prognosis and plan of operative procedure.

5. The use of roentgenography and fluoroscopy is of great value in determining the position and extent of the exudate.

6. Local analgesia is the method of choice except in children where open drop ether may be necessary.

7. Improvement in constitutional symptoms following operation for postpneumonic cases in our series was usually prompt; while in postinfluenzal cases four or five days elapsed before similar improvement was attained.

8. Balcony treatment, blow bottles, deep breathing, and chest and arm exercises should be instituted early in the convalescence.

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TUMORS OF THE BREAST*

BENIGN AND MALIGNANT—A REVIEW OF 331 CASES

CHARLES H. PECK, M.D., AND
WILLIAM CRAWFORD WHITE, M.D.

THIS record includes 331 cases of tumor of the breast, 136 being benign tumors (41 per cent) and 195 malignant tumors (59 per cent).

The majority of these cases have been treated on the second surgical division of The Roosevelt Hospital, the remainder being outside private patients of the authors. It is convenient to consider each group separately.

Benign Tumors and Cysts. Analyzed from the pathologic standpoint, this group consisted of:

	Cases
Single cysts	23
Localized cystic mastitis	18
Generalized cystic mastitis	13
Papillary cystadenoma	9
Galactocele	2
Adenofibroma	50
Intracanalicular fibroma	14
Tuberculosis	3
Lipoma	2
Hematoma	2
	136

The single cysts were for the most part the typical blue-domed cyst of Bloodgood, which we find a relatively common lesion and believe to be always benign. That such cysts may be associated with carcinoma in the adjacent breast tissue, or at a distance, we do not doubt, but such association has not been observed in this series.

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The operation of choice is local excision, including just enough adjacent breast tissue to insure complete removal of the cyst wall, which is so thin and adherent as to make true enucleation difficult or impossible.

None of the cases followed has developed malignancy, and in 1 case only was secondary operation for another cyst, one year later, required.

Localized Cystic Mastitis. The cases of localized cystic mastitis, 18 in number, differ in that more than one cyst, sometimes several of varying size, occur in a localized area of the breast, forming a distinct lump.

In this group a V-shaped wedge of breast tissue is excised from the deep surface, including the affected area; the incision being carried through normal breast tissue on either side. After careful hemostasis, the cut breast tissue is carefully coapted by fine catgut sutures, placed separately through the anterior and deep capsule, including enough breast tissue to secure accurate apposition and prevent the formation of an hematoma.

This restores the contour of the breast and is done preferably through a curved incision at the lower border, the breast being reflected upward and the dissection done from the deep surface. The patient should always be warned that a lump will be felt in the breast at the site of excision, which will disappear by absorption in a few weeks' time. The cicatrix is covered by the overhanging breast and is usually quite invisible to ordinary inspection unless the breast is lifted. Two cases in this group developed later a similar lesion in the opposite breast, requiring secondary operation. One case had both breasts involved primarily.

We have long believed that unnecessary mutilation by the performance of radical operations for these distinctly benign conditions was unwarranted, and speaks for lack of ability or confidence in diagnosis by the surgeon, rather than consideration for the future comfort and safety of the patient.

The advice and support of a trained pathologist at the operating table, with frozen sections when in doubt of the nature of the process, is essential to the best interests of the patient in the modern treatment of breast tumors.

General Cystic Mastitis. There were 13 cases of general cystic mastitis in which the distribution of the cysts necessitated complete removal of the gland.

The Warren incision is used by preference, the breast being reflected upward and the entire gland removed from the deep surface. Occasionally only a part of the cysts will be tense enough to form palpable tumors, other flaccid or partly filled cysts being scattered throughout the remainder of the gland.

By conserving enough of the subcutaneous fat to build up a pad beneath the nipple by deep sutures, flattening and deformity when healing is complete, can be greatly diminished.

Papillary Cystadenoma. Our belief that this lesion is essentially benign has been greatly strengthened by Bloodgood's valuable studies and contributions to the literature of this subject. This does not apply to smooth-walled cysts with bloody content, which are essentially malignant and should be so treated.

From a pathological viewpoint there does not seem to be any indication for a radical operation on papillary cystadenomata, whether young or old. We have not seen any carcinomatous changes along with any of our papillary cysts. Our radical operations for this condition were due to the earlier impression that they were potentially malignant. Clarke and Stout report that they have never seen malignancy develop from papillary cystadenoma.

Bloody Discharge from the Nipple. Blood-stained discharge from the nipple without a palpable mass is not evidence of malignancy and does not call for operative interference. With the presence of a tumor it calls for operation.

Of our 9 cases of papillary cystadenoma 2 had bloody discharge from the nipple. Complete mastectomy was performed in 6 of the 9 cases, in 5 of which axillary dissection was also done. The remaining 3 were treated by local excision. The high percentage of radical operations in this group occurred in our earlier cases when we had greater fear of their potential malignancy.

Galactocele requires little comment; it is quite benign, and simple enucleation of the cyst is all that is called for.

It is relatively infrequent, only 2 cases appearing on our records.

Adenofibroma. This group is the most important of the benign lesions as to diagnosis and selection of operative procedure.

Differentiation of types can be carried to an extreme, and pathologic variations are so numerous as to almost defy classification. A broad general distinction, however, can be made between growths which are distinctly encapsulated and those which are not.

Encapsulated Adenofibroma. The encapsulated forms are benign and local excision is adequate and safe, even if the histologic type is so cellular as to engender the fear of possible malignant tendency. We believe that this is a safe statement and it is a viewpoint which Bloodgood emphatically supports. Two cases had tumors in both breasts and 1 had a secondary operation one month later for a nodule probably overlooked at the primary operation. No case followed developed subsequent malignancy.

Non-encapsulated Adenofibroma. Non-encapsulated adenofibroma, with or without cystic changes, occupies the borderland, and great care must be taken if such cases are classed as benign, and treated on this assumption. Nevertheless, many cases of this type are nonmalignant, and with proper pathologic examination, immediately done by a competent pathologist, may be safely so considered. The gross appearance of the cut tissue is, as a rule, a better guide to its nature than even a frozen section, though the latter should always be used in doubtful cases. Pathologists of the widest experience, e. g., Ewing, Bloodgood, Clarke and Stout, etc., concur in this opinion.

In this type of lesion other clinical factors must be considered: the age of the patient; the possibility of future pregnancy and lactation; the relative amount of glandular tissue involved; in deciding whether local excision is safe and desirable; whether complete removal of the breast, sparing skin and nipple, is sufficient; or the typical radical operation as for cancer should be performed.

The 2 cases in our benign series in whom cancer developed later were of this type, and in both the complete radical operation was performed primarily.

We are greatly indebted to Bloodgood for his exhaustive and sane analysis of the pathology of this group, published in the *Archives of Surgery* of October, 1921.

In 2 of the cases in this group the breast was completely removed without axillary dissection, and in 4 a complete radical operation was performed.

Multiple tumors in a breast are usually adenofibromata, cysts or tuberculosis. Primary malignant tumors are rarely multiple.

Intracanalicular Fibroma. Our 14 cases in this group were all encapsulated, offered no special difficulties in diagnosis and were treated by enucleation or local excision. This lesion is always safely classed as benign.

Tuberculosis. There were 3 cases only of this lesion. One case operated upon in April, 1912, for multiple masses in the right breast, had a similar process develop in October, 1912, in the left breast, which was also removed. Last examined in February, 1920, she was perfectly well and is believed to be so at the present time. She had a child four years before operation.

A second case is well seven years postoperative and the third died six years postoperative of a nontuberculous malady.

Two cases of lipoma and two of hematoma were included in the records, but require no special comment.

There were 4 secondary operations in the series already cited; 1 for single cyst, 1 for local cystic mastitis, 1 for adenofibroma and 1 for tuberculosis.

Two cases developed carcinoma, but in both, as already stated, the primary operation had been of the complete radical type.

Except for those 2 cases there have been no late deaths in any way connected with the breast lesion as far as known, and there was no immediate mortality in the series. Some of the other facts noted were as follows:

Sex.	Males:	8
	Females:	128
	Of the females:	44 were single
		76 were married
		8 were widowed
		8 not recorded

The patients who had lactated numbered: 39
The patients who had not lactated numbered: 62
Not stated: 35

Bleeding from the nipple was recorded in 6 cases:
2 of papillary cystadenoma
1 of local cystic mastitis
3 of adenofibroma

The types of operations performed were:

Complete Mastectomy	15 cases
(Skin and nipple was left in 10 cases)	
General cystic mastitis	8
Local cystic mastitis	1
Single cyst	2
Adenofibroma	4
Papillary cystadenoma	1
Tuberculosis	1
	15 cases
Complete Mastectomy with Axillary Dissection	19 cases
The conditions for which this was done were:	
General cystic mastitis	4
Local cystic mastitis	4
Adenofibroma	2
Papillary cystadenoma	5
Tuberculosis	2
	19 cases
Partial Mastectomy	12 cases
Local Excision or Enucleation	90 cases
Total	136 cases

The types of incision were:

Curved at lower border	85
Radial	16
Curved at areola	1
Oblique ovoid	22
Transverse ovoid	12

Summary. (1) Benign tumors or cysts of the breast can be definitely diagnosed at the operating table in a high percentage of cases, and should be treated by conservative surgical procedures. Mutilating radical operations for such conditions are unnecessary and are a confession of ignorance or timidity on the part of the surgeon.

(2) A trained pathologist should be present at the operating table to assist the surgeon in determining at once the nature of the pathologic process.

(3) Cysts of the blue-domed type and localized and generalized chronic mastitis are neither malignant nor precancerous conditions and should not be so considered.

(4) Non-encapsulated tumors of the adenomatous type form a borderline group. They are by no means always precancerous lesions and in younger women radical operations should be avoided if possible. In older patients, and when the amount of breast tissue involved is considerable, radical operation may be indicated.

(5) Multiple primary tumors or cysts are rarely malignant. Possible exceptions to this rule, e. g., a carcinoma developing in a breast already the seat of a benign tumor, have not been observed in this series. This rule does not apply to advanced cases of carcinoma with outlying nodules which are really secondary deposits.

(6) Conservative operations should, when possible, preserve the contour of the breast, and incisions should be so placed as to leave an inconspicuous cicatrix.

The curved incision at the lower border (Warren) best meets this requirement.

MALIGNANT TUMORS OF THE BREAST

There were 195 cases of malignant disease of the breast in this series, of which 4 were sarcoma and the remaining 191, carcinoma.

Of this number follow-up reports have been obtained in 118, 59 being dead, or alive with recurrence; 53 are alive and well at the present time, 27 of the latter having passed the five-year mark; 6 postoperative deaths occurred while the patients were still in the hospital.

The unexpected sources from which some of our follow-up information has come would indicate that probably not all of the 77 untraced cases are dead, though the proportion cannot be stated. To cite an illustration, within the past fifteen months, two sisters, operated upon in 1910 and 1912, respectively, from whom no report had been received

for several years, were both found to be quite free from recurrence when one was brought to the hospital for acute perforative cholecystitis in October, 1920. Cured patients often wish to forget their unpleasant experience and fears, and avoid reporting to the surgeon for fear of something wrong being found.

One can hardly speak of percentages of cures with so many cases untraced, nevertheless the results show some measure of encouragement in spite of this fact.

There were 6 deaths from the immediate effects of the operation: 3 due to embolus on the seventh, tenth and fourteenth days postoperative, respectively. One died of shock within twelve hours. One died of cardiac failure due to preëxisting cardiac disease on the fourth day. One died of wound sepsis on the seventeenth day.

In regard to the operative procedure, the following facts have been tabulated:

Complete mastectomy with axillary dissection was done in all of the 195 cases.

Excision of the thoracic portion of the pectoralis major muscle in 186 cases.

Excision of the pectoralis minor muscle in 71 cases.

Division of the pectoralis minor muscle with resuture in 54 cases.

Excision of a part of the sheath of the rectus abdominis in 23 cases.

Plastic or sliding flaps in 8 cases.

Skin graft in 5 cases.

The oblique ovoid incision, or some modification of it, was done in 114 cases.

The transverse ovoid incision of Stewart was done in 81 cases.

The transverse incision of Stewart has been the operation of choice for some six or seven years past. The resulting scar is well placed and does not encroach on the shoulder or arm; there are no cords of cicatrix to interfere with free arm motion; the exposure of the axilla to its highest point is excellent. The direction of the incision facilitates sliding upward of the lower flap so that skin grafting is rarely necessary, even after removal of larger areas of skin. The

pectoralis minor is usually preserved either by division and resuture, or better, by retraction for axillary dissection.

We believe that it tends to protect the axillary vessels from constricting cicatrices and minimizes the danger of edema of the arm which we rarely see in a marked degree.

We employ block dissection from above and within downward and outward, following the plane beneath the pectoralis major and removing the sheaths of pectoralis minor and serratus magnus. The axilla is drained through a stab wound. We do not excise the supraclavicular glands, having felt that if the disease has involved this group the prospect of a radical cure is slight.

We have not made a special point of excising a portion of the sheath of the rectus abdominis, though it has been recorded in 23 of the series and has probably been done in a larger number without mention in the history. It is usually done when it comes naturally in the field of a wide block dissection, as is frequently the case.

We follow the teaching of Handley in making a wide oblique dissection of subcutaneous fat well out beyond the edges of the skin incision, thus removing a greatly augmented area of subcutaneous tissue and muscle sheath.

We believe that extension by diffusion in all directions from the primary growth, especially in the lymph-spaces of the subcutaneous tissue, is a factor of importance.

In doubtful cases the tumor is completely excised with a safe margin of adjacent tissue and immediately cut and inspected by a pathologist and the operating surgeon.

In the majority of malignant tumors gross inspection of the cut surface is quite sufficient to determine the diagnosis, but if doubt exists the result of a frozen section is awaited. We feel that a frozen-section diagnosis is of great value in some of the doubtful cases. It should always be interpreted, however, in conjunction with the appearance of the gross section, the presence or absence of encapsulation and the general clinical picture.

Delayed Radical Operation. We have had 11 cases in which the primary excision of the tumor was followed at an interval of days or weeks by radical operation as a result of pathologic findings: in 7 cases the interval was from three

to seven days; in 2 cases two weeks; in 1 case four weeks and in 1 case three months. Of the 9 cases followed, five are alive and well at ten months, eighteen months, five years, eight years and ten years, respectively; 4 died or had recurrence at four months, nine months, one year and four years, respectively. Two cases have not been traced.

Delayed radical operation after excision of the tumor for diagnosis is never the procedure of choice, but as our results show, is not invariably followed by fatal recurrence; in fact, though the number of cases is small, the percentage of cures is quite as large with the other methods.

Diagnostic Points. The history of the length of the time the tumor has been observed, we have found to be of little help. The same may be said of the lack of retracted nipples, adhesions to the superficial or deeper tissues, palpable axillary lymph-nodes, pain and tenderness or history of trauma. Presence of retracted nipples and adhesions to

TABLE 1

LOCAL EXPLORATORY WITH SECONDARY OPERATION LATER

	Interval	Tumor	Present
1	2 weeks	Medullary no metastasis	O.K. ten years
2	3 months	Adenocarcinoma with metastasis	Died one year later
3	7 days	Adenocarcinoma with metastasis	Recurrences four months later
4	27 days	Medullary carcinoma no metastasis	O.K. ten months
5	2 weeks	Adenocarcinoma no metastasis	O.K. eighteen months later
6	3 days	Scirrhous carcinoma with metastasis	O.K. eight years
7	4 days	Scirrhous carcinoma with metastasis	Died nine months later
8	6 days	Medullary with metastasis	Died four years later
9	2 weeks	Adenocarcinoma no metastasis	O.K. five years
10	3 days	Scirrhous carcinoma no metastasis	Lost
11	1 week	Medullary no metastasis	Lost

Metastasis means axillary involvement.

the superficial tissue, as shown by the orange-peel appearance, on the contrary, are of great help. Axillary nodes are often palpable in benign tumors and often not palpable in malignant tumors. The sense of hardness is often of some help,

while multiple primary nodules rather point toward a benign condition, but not absolutely so.

When cut open after the tumor has been excised, one may be influenced by the gritty hard feeling to the knife, the absence of capsule and the minute yellow dots.

In the case of a sarcoma, one is more dependent upon a frozen section, because the gross picture is often confused with an edematous adenofibroma.

We have not had any malignant tumor in a patient under twenty-five years of age, but in the presence of absolute signs we would not hesitate to do a radical operation in a young woman under that age.

The cases described as Paget's disease were frankly malignant, and although they did not perhaps come under the original description by Paget, still we have called them by that name, because of the general custom. Both of these cases were lost to our recall system.

The 1 case of sarcoma that we have followed has been alive for nine years, and is now well. The diagnosis was made by a competent pathologist, but we have no microscopic description or slide of the case.

The carcinomas have been put in three classes, although it is admitted that it is not a division into very distinct groups, and our recall notes do not help us show that there is any particular difference in their virulence, in spite of the general tradition. What we have noted is what we would have expected, that the cases without metastases have a better outlook.

We have used postoperative *x*-ray treatment as a routine procedure for the past three or four years, but the cases are too recent to draw conclusions from. We believe that it is good insurance and may retard or prevent recurrence in certain cases. We also advise *x*-ray or radium when recurrence is actually present, and think it effects retardation of the growth and often gives increased comfort, but up to the present time we have seen no cases cured.

TABLE II

RECURRENCES OR DEATHS

Years	Adenocarc. with metastasis	Adenocarc. without metastasis	Scirrhous carc. with metastasis	Scirrhous carc. without metastasis	Medullary carc. with metastasis	Medullary carc. without metastasis	Carcinoma with metastasis	Cancer with metastasis	Cancer without metastasis
0	8	0	1	1	3	0	0	12	1
1	9	3	1	0	5	1	1	16	4
2	2	0	3	2	3	0	0	8	2
3	3	0	0	0	3	1	0	6	1
4	1	0	0	2	1	0	0	2	2
5	0	1	0	0	0	0	0	0	1
6	1	0	0	0	0	0	0	1	0
7	1	0	0	0	0	0	0	1	0
8	0	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0	0
11	1	0	0	0	0	0	0	1	0
12	0	0	0	0	0	0	0	0	0
13	0	0	0	0	0	0	0	0	0
14	0	0	0	0	0	0	0	0	0
15	0	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0	0
18	0	0	0	0	0	0	1	1	0
								48 cases	11 cases

A study of the histories of the 195 cases brought out some facts of interest in history and physical examination; only positive statements are recorded:

57 cases had retracted nipples.
16 cases had ulcerated skin areas.
94 cases showed adhesion to the skin.
31 cases showed adhesion to deep muscles.
9 cases showed multiple nodules (mostly advanced cases with secondary nodules).
77 cases showed palpable axillary nodes.
109 cases showed axillary nodes involved at time of operation.
70 cases had lactated previously.
68 cases had not lactated previously.
15 cases gave a history of previous trauma.
15 cases complained of pain and tenderness.
There was only 1 male in the series.

Analysis of the pathologic findings and their relation to results as shown in the tables is of considerable interest:

TABLE III

NO RECURRENCE, ALIVE AND WELL JUNE, 1922

Years	Adenocarc. with metastasis	Adenocarc. without metastasis	Scirrhous carc. with metastasis	Scirrhous carc. without metastasis	Medullary carc. with metastasis	Medullary carc. without metastasis	Carcinoma with metastasis	Carcinoma without metastasis	Total cancer with metastasis	Total cancer without metastasis
0	1	0	2	2	1	3	0	0	4	5
1	2	3	0	1	0	2	0	0	2	6
2	0	0	1	2	0	1	0	0	1	3
3	0	2	0	2	0	0	0	0	0	4
4	0	0	0	0	0	1	0	0	0	1
5	0	1	1	1	3	0	0	0	4	2
6	0	2	0	0	0	1	0	0	0	3
7	1	1	0	0	2	2	0	0	3	3
8	0	2	1	0	0	0	0	0	1	2
9	0	1	0	1	1	0	0	1*	1	3
10	0	1	0	0	0	0	0	0	0	1
11	0	2	0	0	0	0	0	0	0	2
12	0	1	0	0	0	0	1	0	1	1

* 1 equals fibrosarcoma

Cancer with metastasis.....17 } 53
Cancer without metastasis...36 }

78 cases were classed as adenocarcinoma.
53 cases were classed as scirrhous carcinoma.
58 cases were classed as medullary carcinoma.
2 cases were classed as Paget's disease.
4 cases were classed as sarcoma.

Of the 59 cases traced which died or have recurrences, 48 cases had axillary glands involved at the time of operation; 11 cases had no axillary-gland involvement.

Of the 53 cases now alive and well, 17 had axillary glands involved; 10 of these are well more than five years; 36 cases had no axillary involvement; 17 of these are well more than five years.

Cases Operated Upon Before January 1, 1917 (more than five years ago).

We have definite follow-up information on 69 cases operated upon more than five years ago. Of these there are:

Dead, or alive with recurrence		42
With axillary metastases at time of operation	33	
Without axillary metastases at time of operation	9	
	42	
Alive and well		27
With axillary metastases at time of operation	10	
Without axillary metastases at time of operation	17	
	27	
		69

A study of this group shows that our percentages correspond closely with those reported by Sistrunk and McCarty in the *Annals of Surgery* for January, 1922; of our 69 cases there were:

Alive and well more than five years	39 per cent
Alive and well more than five years; cases with metastases	23 per cent
Alive and well more than five years; cases without metastases	65 per cent

EXTRAUTERINE PREGNANCY

CLINICAL ANALYSIS OF 108 CASES*

GRANT P. PENNOYER, M.D.

THIS paper is simply an analysis of the history, symptoms, treatment and results of 108 cases of extrauterine pregnancy treated in The Roosevelt Hospital. The dates of admission fall between January 1, 1913 and January 1, 1921, except for one case of special interest, which will receive individual comment. Thirteen of the 108 cases were treated by the general surgical divisions, all but one because of a mistaken preoperative diagnosis. The individual case mentioned was on the medical division. All the rest were treated by the gynecological division in charge of Dr. Howard C. Taylor.

In the eight years covered by this report, there were 5763 gynecological operations performed at The Roosevelt Hospital. As 108 of these were cases of ectopic pregnancy, this disease represents 1.84 per cent of the total number. Wynne, in his long series, covering twenty-seven years, finds this per cent to be 1.3 and Farrar finds it 1.5. The condition is therefore far from being a rare disease.

The age distribution is as follows:

Below 20 years	1 case
20–25 years	12 cases
25–30 years	36 cases
30–35 years	32 cases
35–40 years	19 cases
40–45 years	5 cases
Over 45 years	0 cases
Age unknown	3 cases

The findings of the other authors are remarkably similar. I do not believe that this is of any more significance than that the disease may occur at any time during the childbearing period. There seems to be no traceable connection

* This paper was written especially for The Roosevelt Hospital Report, 1924.

between the condition and the length of time which has elapsed since the patient's marriage. Of the 108 cases, 5 were unmarried and 3 were widows, making 7.4 per cent of the total illegitimate pregnancies.

The question of previous pregnancies is of more interest. This is unknown in 5 cases. Of the remaining 103, only 15 cases had never been pregnant before, while the remaining 88 or 85 per cent had all had previous uterine pregnancies. 79 had had children and 9 had had one or more miscarriages. 62 cases had had no miscarriages and the other 41 had had at least one. Only 26 of the 88 cases who had had previous normal pregnancies had had but one pregnancy. These figures correspond almost exactly with the findings in other series. Brady finds that 88 per cent had had previous uterine pregnancies; Frank, 85 per cent; Farrar, 85 per cent; Wynne, 79 per cent.

As infection of the uterine tubes is especially frequent at the time of delivery, or miscarriage, this constant predominance of the cases who had had previous pregnancies may be of significance for that reason. However, only 7 of our cases give a definite history of infection following the labor or miscarriage. This may be a matter of incomplete record. Possibly this predominance is partially a result of chance. If ectopic pregnancy is simply an accident that may occur in any child-bearing woman, it seems reasonable to suppose that the majority of cases would occur in other pregnancies than the first.

The interval of time elapsing since the last pregnancy is of significance. This, too is very similar in the other series reported in the literature. Of our 88 cases who had had previous pregnancies, the time which had elapsed since the last pregnancy is as follows:

1 year or less	16 cases
1 to 2 years	15 cases
2 to 3 years	8 cases
3 to 5 years	14 cases
5 to 10 years	22 cases
10 to 16 years	9 cases
Unknown	4 cases

The disease may occur immediately after a normal pregnancy, but is more apt to occur a very considerable time later. Enough cases follow soon after a normal labor to make this point of little value in diagnosis, but even a period of sixteen years or more since a pregnancy does not rule out the condition. The average time is nearly five years.

The number of cases who had had a previous salpingitis is difficult to determine. Using as evidence both the history and the operative findings, we find 39 cases, or 38 per cent, had had inflammation of the uterine tubes; 63 had not, and 6 were doubtful. Brady reports only 14 per cent giving evidence of previous salpingitis; Oatsler, 31 per cent. Undoubtedly many of the cases with negative histories and operative findings may have had previous inflammation of the tubes, and these figures are unreliable. Pelvic inflammatory disease may frequently be an etiological factor.

Eighteen cases had had previous abdominal operations, no particular operation being especially more frequent. Only one case had had a previous ectopic gestation. Abdominal surgery is so frequent it seems safe to say that these operations undoubtedly had no relation to the disease.

The menstrual history before the onset also has no relation to the disease. Eighty-eight cases had had no previous menstrual disturbance. Fifteen complained of more or less irregularity, 3 of excessive pain, 2 of excessive flow. This is probably not more than a normal proportion of these disorders.

The menstrual history after the onset of the illness is of much more interest. In 42 of our cases the classical history of delayed menstruation could not be elicited. These women had had what they considered a normal period within a month of the beginning of their illness. Very likely many of them were careless about their dates or considered the vaginal bleeding due to the disease as a normal menstruation, but the fact remains that only a little over half of our cases give the usual history of late menstruation. Oatsler finds 50 per cent gave no history of being over-due; Wynne, 44 per cent; Farrar, 35 per cent. Therefore, too much emphasis must not be placed upon this point to make a diagnosis of ectopic pregnancy.

The patients' chief complaint is as follows:

Pain	72
Irregular bleeding	27
Irregular bleeding and pain	5
Prostration	3
Tumor	1

This corresponds very closely with the other series.

The first symptom particularly noticed by the patient is as follows:

Irregular bleeding	57
Pain	47
Fever	1
Amenorrhea	3

The small number of cases first noticing amenorrhea is remarkable, as this is sometimes considered the first classical symptom.

The average duration of this first symptom at the time of admission to the hospital was twenty-eight days. Two cases with coincident pelvic inflammatory disease complained of symptoms of over nine months' duration, which had recently grown worse. The shortest duration was two and a half hours and 3 others were less than twelve hours. Two cases were four months, and 12 were two months or more.

Pain and vaginal bleeding are by far the most constant symptoms of the disease. Pain ranks first at 96 per cent in our series. Only 4 cases gave no history of pain. Brady finds 96 per cent had pain in some form; Frank, 98 per cent; Wynne, 99 per cent; Farrar, 96 per cent. In our 4 cases giving no history of pain, 3 of them were unruptured, and in none of them was the correct diagnosis made preoperatively. One case which was ruptured and had free blood in the peritoneal cavity gave no history of pain. Twenty-three cases gave a history of sudden violent pain without any previous disturbance, all but one of which were ruptured. Seventeen cases had had a sudden violent attack of pain following same sort of previous pain. All but one of these were ruptured. The remaining 54 cases had had no sudden violent attack, but had either cramps or some variety of pain. Of the total 104 cases, who had had pain, 41 did not localize it more definitely than the lower abdomen. Three

called it general abdominal and 2 referred it to the back, but all the remaining 58 localized it in either the right or left lower quadrant of the abdomen. However, in 6 of this last group, the tube affected was on the opposite side. Thus, though pain is almost a constant symptom, its nature and location is variable.

Only 18 cases of the 108 had had no vaginal bleeding. Fifteen of these were ruptured, and 3 were unruptured. Thus, over 83 per cent had more or less vaginal bleeding. Frank finds this per cent 94, Brady, 74 per cent, and Oatsler, 90 per cent.

All other symptoms are much less constant. Fourty-four cases had had nausea or vomiting; 23 cases, all ruptured with intraperitoneal bleeding, were more or less prostrated. Twenty-eight cases showed some sort of bladder irritation such as frequency of urination, dysuria, etc. Seven had definite breast changes, 12 possible breast changes. Four had some sort of rectal irritation.

The physical examination and laboratory findings show very considerable variations. The pelvis in 10 cases was considered normal to digital examination, and all these cases were operated upon by the surgical divisions under a mistaken diagnosis, usually acute appendicitis. Ninety-two cases had an abnormal pelvic mass, and the remaining 6 had at least tenderness in the fornices of the vagina. Softening of the cervix or lower uterine segment is often a doubtful finding, but was mentioned in 53 cases.

The temperature and leucocyte count of the blood in uncomplicated cases seemed to be closely associated with intraperitoneal hemorrhage, especially its amount, rapidity and duration. The more extensive and rapid the hemorrhage, the higher the temperature reaction and the leucocytosis. The amount of fever is usually very moderate. Only 3 cases reached as high as 103°, and 2 of these were complicated by pelvic infections. Of all the other cases showing fever, only 3 reached 102°. However, only 15 of the 80 cases with free blood in the abdominal cavity failed to show a temperature of at least 99.2. Generally the temperature was 100° to 101°. Four of these exceptional cases had subnormal temperatures, because of extreme shock. All the

remaining 11 were cases in which the bleeding was over one week's duration. Of these same 80 cases with abdominal bleeding, only 20 failed to show a leucocytosis of at least 10,000, and all these 20 were also cases where the hemorrhage was over one week old. The highest leucocytosis was 30,000, 86 per cent polynuclear type. The hemoglobin and the red cell count fall with hemorrhage. The lowest hemoglobin was 26 per cent, and the lowest red cell count was 1,300,000.

The difficulties of diagnosis are illustrated by the following facts. In only 45 cases, or less than 42 per cent, was a positive preoperative diagnosis made. In 14 cases, ectopic pregnancy was mentioned as less probable than some other condition, especially pelvic inflammatory disease. Twenty-six cases were diagnosed as pelvic inflammatory disease, 13 as appendicitis, 4 as incomplete abortion, 2 as dead uterine pregnancies, 6 as ovarian cysts, 1 as chronic endometritis. In the remaining 13 cases the preoperative diagnosis was not definitely mentioned. Twenty-five cases had a posterior colpotomy performed to insure the diagnosis before the abdomen was opened. Twenty-six cases had a dilatation and curettage before the abdomen was opened. Four cases had had a dilatation and curettage before admission (2 in other hospitals) and had been discharged as cured.

The time the patient was in the hospital before operation is very variable. If the patient is not actively bleeding, even though the diagnosis seems certain, the case is not considered one for immediate operation. Thirteen of the cases operated upon within a few hours of the patient's admission were done by the surgical divisions as cases of acute appendicitis. The average length of time this group was in the hospital before operation was only six and a half hours. The patients who were in the hospital longest were those considered to be suffering from pelvic inflammatory disease. The average length of time these 26 cases waited in the hospital before being operated upon was nine days, the shortest one day, the longest thirty-two days. When the case was recognized as one of ectopic pregnancy, the patient was operated upon much more promptly. Nine cases had symptoms of active internal hemorrhage when admitted and were operated upon immediately. The average time

these patients were in the hospital before operation was only two and a half hours, the shortest thirty minutes and the longest four hours. The remaining 50 cases considered as probable ectopic pregnancies before operation were only in the hospital on the average of two and a half days before operation. These patients were operated upon as soon as was convenient, usually on the morning after admission.

A complete or partial salpingectomy was done in all the 106 cases operated upon. Numerous additional operations were done according to the indication and are hardly worth tabulating. Thirty-six cases had appendectomies, several oophorectomies, hysteropexies, a few hysterectomies, 87 cases were ruptured, 21 unruptured. This predominance of ruptured cases was found by all the other authors and is to be expected, as it is usually the symptoms of rupture that bring the patient to a doctor. Eighty of these cases had diffuse intraperitoneal hemorrhage, the other 7 had encysted hemorrhage; all of long duration. Sixty-two cases were on the right side, 46 on the left. One was in the ovary and one was interstitial; 23 cases had had tubal abortions. These findings correspond closely to the other series.

Of the 106 cases operated upon, one died of pulmonary embolus on the tenth day postoperative, one died of postoperative pneumonia on the twenty-sixth day, one died from peritonitis on the twenty-first day and only one died immediately postoperative from hemorrhage and shock. The remaining 102, or about 97 per cent, were discharged as cured.

There were 2 fatal cases not operated upon. The diagnosis in both of these was made by autopsy. One of them had a complicating infection and died from general peritonitis, two days after admission. She was in a critical condition on admission. The second case is of particular interest, as it is the only case dying from hemorrhage alone. The patient (History F–19538) was a married woman of twenty-five who was admitted to the medical ward in a moribund condition with a diagnosis of pneumonia, and died within an hour. She had been sick only three days. She had had some abdominal pain, but the most marked symptom from the first had been extreme prostration. She had had no menstrual

disturbance except for a slight bleeding, starting with her illness. This was considered a normal menstruation as it was on the expected date for a normal period. She had had no previous pelvic disease and one normal pregnancy two years before. The abdomen was distended with fluid, the lungs were filled with moist rales. The temperature was 103, the pulse 140, the hemoglobin 30 per cent, the red blood cell count 1,300,000, the leucocyte count 30,000, 86 per cent polynuclear type. The autopsy revealed that the woman had died from hemorrhage from a ruptured ectopic. The most interesting feature of this case was the short duration of the pregnancy. The whole mass was a fusiform swelling in the center of the right tube, hardly $1\frac{1}{2}$ cm. in diameter, and the rupture was less than $\frac{1}{2}$ cm. long.

Thus in the total 108 cases, there were six deaths, or not quite 95 per cent were discharged as cured. Wynne reports a mortality of 4.3 per cent; Frank, 3.75 per cent; Oatsler, 6 per cent; Farrar, 1 per cent. The disease, therefore, with good hospital care, has an extremely low mortality. Fatal hemorrhage, the usually dreaded accident, occurred in but one case.

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TUBERCULOUS DACTYLITIS*

EDWARD SHERRARD RIMER, M.D.

DACTYLITIS or spina ventosa is essentially a disease of early childhood, affecting the phalanges, less commonly the metacarpal and metatarsal bones. It tends to spontaneous and almost complete recovery.

HISTORY

An Italian boy, aged two years, was admitted to Bliss Ward of Roosevelt Hospital on May 2, 1923. The child was suffering from swelling of fingers (six weeks' duration[2]) cough (four months' duration following whooping-cough) and persistent nasal discharge (five months). Nodules in the skin about thighs and arms had been noticed two months previously. Conjunctivitis had persisted for one month. The voice had been hoarse for two months.

Family History. Father was thin; working every day, but had had a cough for ten years. The mother had had one miscarriage. Two brothers, aged nine and seven respectively, were both living and well. A neighbor's child had a chronic cough.

Past History. The patient was a full-term infant, normal delivery, was normal at birth. Birth weight was 7½ lbs. Was breast-fed up to twenty-three months. The first teeth appeared at seven months. He walked at nine months, and talked at one year. His appetite was fair. Bowels irregular. Sleep quiet.

He was said to have had scarlet fever at seven months and whooping-cough four months ago. He has frequent colds and is sickly most of the time.

* This paper was written especially for The Roosevelt Hospital Report, 1924.

EXAMINATION

Physical examination shows him to be a fairly well-developed, but pale and poorly nourished, child. The voice is hoarse and he cries or whines most of the time.

The *skin* is dry and loose, and the muscles flabby. Subcutaneous fat is diminished. The lymph-nodes are small, but palpable in the neck, axillae and groins.

Head. The fontanelles are closed. The conjunctivae are injected. Purulent discharge from right eye. Pupils are equal and react normally. There is a strabismus of the left eye. Ears are negative. Nose, purulent discharge present. The lips are deeply fissured. Eighteen teeth are erupted. Tonsils are moderate in size. Throat clear.

Chest. Flat; poor expansion. Heart not enlarged. Soft systolic at base. Lungs: Right upper anteriorly fremitus increased. Breath sounds diminished over left upper posteriorly. Intrascapular dulness noted. D'Espine negative. Bronchovesicular breathing at lower angle of scapula. A few moist rales at both bases.

Abdomen. Soft, not distended. Liver 3 cm. below costal margin. Spleen hard, sharp; border at level of umbilicus.

Reflexes were active. Kernig negative. Neck sign negative.

Skin. Hard round nodules about the size of a pea attached to skin. Not inflamed, but one or two purplish in color, on thighs, legs, forearms; a smaller one on back of right hand.

Extremities. Spindle-shaped swellings of fingers, red but not tender, were noted: right hand, index, second phalanx; middle, first phalanx; thumb, first phalanx. Left hand, little finger, first phalanx.

The *weight*, on April 14, 1923, when first seen at University & Bellevue Hospital Medical College Children's Clinic, was 22 lbs. 9 oz. The child was admitted to Roosevelt Hospital on May 2, 1923. On May 6th, the weight was 20 lbs. 10 oz. on May 13th, 21 lbs. 1 oz. On discharge, May 20th, it was 21 lbs. 4 oz.

On May 5th, Pirquet++, Schick++, Wassermann negative. R.B.C. 5,000,000. W.B.C. 10,000. Poly. 74 per cent, Hb. 70 per cent. No malaria. The urine was negative.

Temperature range was 98–99 (103 on May 4th. Normal next day).

Respiration range 24–30.
Pulse range 120–128.

X-ray Report. "Peculiar marked mottling in both hilus and peribronchial regions. Apparent cardiac enlargement to left. The process suggestive of either bronchopneumonia or possible hilus tuberculosis." Dr. LeWald at College Clinic.

DIAGNOSIS

1. Dactylitis—tuberculous.
2. Rhinitis—chronic.
3. Conjunctivitis—acute.
4. Nodules (described by Wenda as "Nodular tuberculosis of the hypoderma").
5. Pulmonary tuberculosis.

Course. During his stay in the hospital the child's condition improved. The conjunctivitis disappeared, the cough left him, the nasal discharge cleared up, the appetite improved. The child looked better and became brighter and apparently contented. There was little change in the size of the affected digits, but the inflammatory condition subsided somewhat. The nodules in the skin appeared unchanged in any way.

The treatment while in the hospital was directed first toward general measures—proper diet, regular meals, rest in bed. Second, the child was kept out on the roof in the open air practically all the time. The hands were exposed to the sun in gradually increasing periods. The weather was inclement and complete exposure was not given. No specific treatment other than this was given, and the improvement is attributed largely to heliotherapy and fresh air.

He was discharged on May 20, 1923.

CONCLUSIONS

The diagnosis of tuberculous dactylitis is based on the history of probable exposure, the chronicity, the absence of local symptoms of syphilis, the afebrile course, the asymmet-

rical distribution, the positive Pirquet reaction and the negative Wassermann. The prognosis under good hygienic surroundings is for complete recovery. Rarely is operative interference indicated. Fresh air and exposure to the sun's rays for gradually increasing periods of time appear to be effective means of treating the disease.

CANCER OF THE LARGE INTESTINE*

NOT INCLUDING THE RECTUM AND RECTOSIGMOID

JAMES I. RUSSELL, M.D.

IN reviewing the cancerous growths of the large intestine, not including the rectum and rectosigmoid, occurring in the surgical service at The Roosevelt Hospital during the past six years—1915 to 1920 inclusive—we find there were 47 cases admitted into the service, 42 of whom were operated upon; the other 5 either declined operation or were considered inoperable for various reasons—debility, cachexia, etc., with nonobstructive conditions at the time of examination.

During this same period there were 17,527 operations performed, 55 of which were for cancer of the rectum and rectosigmoid, which are not included in this report, but confirm the fact, though the series is a small one, that carcinoma of the rectum and rectosigmoid is much more frequent than in the entire large intestine from the ileocecal valve to the rectosigmoid juncture. As with cancer appearing in other parts of the human body, cancer of the big gut is a condition of later life, though it may occur at almost any age: our oldest patient was seventy-eight years, the youngest twenty-one years. The former was suffering from acute ileus at the time of his admission into the hospital, his condition was extremely grave, and an immediate enterostomy was done, followed by death four hours later. The youngest, a woman of twenty-one years, had a perforated carcinoma of the cecum with extensive peritonitis at the time of admission; abdominal and vaginal drainage were immediately instituted, at which time the cause of the peritonitis was undetermined. A second operation a few days later disclosed a perforated cancer of the cecum. She died eight days after the first operation.

* Read before the New York Surgical Society, April 27, 1921. Reprinted from *Ann. Surg.*, June, 1921.

Cancer of the large intestine was about equally common in the two sexes, there being 24 men and 23 women. The first signals in the great majority were of gradual onset of which the most frequent were pain and constipation. The onset, however, may be of an alarmingly short duration; two days is our shortest time and two years our longest. The average duration of symptoms until admission into the hospital was about six months.

Given the age of the patient and a carefully elicited history, with undivided attention to the symptoms and the sequence in which they appear, aided by a careful physical examination and the *x*-ray findings, it would seem that a correct diagnosis should be reached at a much earlier time. Yet, on the other hand, we know that a cancerous growth, especially in the cecum where the obstructive symptoms may be long delayed, can reach a considerable size and not infrequently be observed by the patient before the surgeon is even consulted.

It is commonly pain, more or less persistent, but usually recurring in attacks with increasing frequency, constipation becoming more aggravated (only relieved by cartharsis, and this in increasing doses and strength), blood in the stools, or possibly a mass discovered by the patient himself, that prompts the patient to seek advice for relief of his condition. Pain was the most frequent symptom complained of in 36 of our cases; constipation, varying from mild constipation to complete obstipation, the next most prominent symptom in 30 of them. Distention, vomiting, loss of strength and loss of weight occurred with about equal frequency in 17 of them. Hemorrhage from the bowel observed by the patient occurred in ¼ of the 47 cases, i. e., 12 complained of this symptom. Five complained of diarrhea and 2 of epigastric distress.

Tenderness in variable degrees was present in a very large percentage of the cases. A stiffening of the proximal segment of the gut under the palpating hand is a very constant symptom and a valuable aid in diagnosis, as is visible peristalsis if present. A palpable mass was present in over half of our cases, i. e., in 26 of them. The *x*-ray gave positive information in locating the growth and the extent of the con-

striction of the lumen of the gut in the 18 cases in which it was taken.

In 23 of the patients the growth was located in the cecum and ascending colon. In 17 it was located in the splenic flexure, descending and sigmoid colon; and in the remaining 7 in the transverse colon; which distribution gives a very high percentage in the right half of the colon and one that we feel would undoubtedly be different in a larger series of cases.

There were 7 cases of acute ileus which demanded immediate operation, 4 of which died — 3 within thirty-six hours after operation and 1 eight days after operation. A cecostomy was done in 3 cases and enterostomy in 1, and 1 other in which cecostomy was done survived but was in poor condition at the time of leaving the hospital. The two-stage Mikulicz operation was done twice in movable sigmoid growths; both patients survived, and are living and apparently well today, eighteen months after operation. Much can be accomplished where this operation can be applied, as the growth can be eventrated and the obstruction can be relieved at the same time by a very quick and simple operation.

Since diverticulitis and carcinoma of the large intestine both occur most frequently after middle life, it is not unusual to confuse the diagnosis of perforated diverticulitis with perforation of a cancerous growth. Both may be insidious and gradual in onset, with the development of a tender and painful mass, rise in the temperature curve, and a distinct increase in the leucocyte and polymorphonuclear count; or the onset may be sudden, presenting the classical picture of a perforated hollow viscus.

Perforation had occurred in 5 of the cases at the time of admission, twice in the sigmoid and once in the descending colon; in each of which the preoperative diagnosis was supposed to be an abscess from a perforated diverticulitis. All were drained, followed by radical operation later; 1 survived the second operation and was in good condition when last seen. In 2 the perforation was in the cecum; both died, 1 in thirty-six hours and the other in eight days.

The microscopical diagnosis in all cases reported upon was that of adenocarcinoma; the adjacent mesenteric lymph-

nodes were carcinomatous five times and hypertrophic several times, but showing no carcinomatous changes.

Primary resection with end-to-end, lateral or end-to-side anastomosis was done 15 times with 3 deaths, a mortality of 20 per cent. The two-stage operation was done 9 times, 7 of which were of the Mikulicz type; in 2 a colostomy was done followed by excision with lateral anastomosis. There was 1 death, a mortality of 11 per cent. Permanent colostomy was done 3 times with no deaths; cecostomy 5 times with 4 deaths. Six inoperable growths were explored, in 4 of which an anastomosis was done around the growth.

The average number of hospital days in the primary radical operation was thirty-two days; in the two-stage radical operation it was seventy-three days. Nineteen of the patients have been traced to the present writing, 7 of whom have died:

One died six years after operation; 1 died three years after operation; 1 died two years after operation; 1 died one and one-half years after operation; 3 died four months after operation.

One is living six years after operation; 1 is living three years after operation; 1 is living two years after operation; 1 is living one and one-half years after operation; 6 are living one year after operation; 2 are living eight years after operation.

A SHORT ABSTRACT OF THE CASES LIVING

Case I (B5844). Living six years post operation. Had palpable mass in ascending colon. *X*-ray not taken. Enterocolectomy with lateral anastomosis. Pathological report: adenocarcinoma.

Case II (A14317). Living three years post operation. Mass not felt before operation. Annular growth of the transverse colon. No *x*-ray taken. Two-stage Mikulicz operation. Pathological report: adenocarcinoma.

Case III (B11867). Living eighteen months post operation. Has gained considerable weight; is doing full-time work and feels perfectly well. Mass felt in left lower quadrant. *X*-ray positive. Partial colectomy of the descending colon with end-to-end anastomosis. Pathological report. adenocarcinoma; metastasis not stated.

Case IV (A15064). Living two years post operation. Physical examination negative. No *x*-ray taken. Carcinoma of the sigmoid. Two-stage Mikulicz operation. Pathological report: adenocarcinoma; metastasis not stated.

Case V (A16898). Living one year post operation. No mass felt. *X*-ray positive. Carcinoma of the transverse colon. Two-stage Mikulicz operation. Pathological report: adenocarcinoma; gland metastasis.

Case VI (A16702). Living one year post operation. No mass felt. No *x*-ray taken. Was a case of acute obstruction; immediate operation. Growth in the sigmoid. Two-stage Mikulicz operation. Pathological report: adenocarcinoma with gland metastasis.

Case VII (B12471). Living one year post operation. No mass felt. No *x*-ray taken. Carcinoma of the sigmoid. Partial colectomy with end-to-end anastomosis. Pathological report: adenocarcinoma; no gland metastasis.

Case VIII (B12881). Living one year post operation. Mass felt in right lower quadrant. *X*-ray positive. Carcinoma of the cecum. Enterocolectomy with end-to-end anastomosis. Pathological report: adenocarcinoma; gland hypertrophy; no metastasis.

Case IX (B12696). Living one year post operation. Acute obstruction at the time of admission. No mass felt. No *x*-ray taken. Immediate operation. Growth in the sigmoid. Two-stage Mikulicz operation. Pathological report: adenocarcinoma. Gland metastasis not stated.

Case X (A16381). Living one year. No mass palpable. *X*-ray positive. Refused operation. Is still living. Condition poor.

Case XI (B13153). Living eight months post operation. Mass in right upper quadrant. *X*-ray positive. Carcinoma of the hepatic flexure. Enterocolectomy with lateral anastomosis. Has gained 30 lbs. and feels perfectly well. Pathological report: adenocarcinoma with gland metastasis.

Case XII (B13605). Living eight months post operation. Incomplete obstruction. No mass felt. *X*-ray not taken. Growth in the transverse colon. Colocolectomy with lateral anastomosis. Pathological report: adenocarcinoma with gland metastasis.

Our total mortality of 28.7 per cent in all cases operated upon seems very high, but is accounted for in some degree by

the extremely grave condition in which a large number of the patients were at the time of their entrance into the hospital.

There were 7 cases of acute ileus, 5 of which were utterly hopeless. It would seem that the aforesaid mortality should be classed as a cancer rather than an operative mortality, since there were 24 radical operations with but 4 deaths, a mortality of 16.6 per cent. Hence, it is rather the graveness of the condition of the patient than the magnitude of the operation upon which the mortality depends.

It should be proved in all cases of suppurative diverticulitis that the perforation is not of cancer origin.

Radical excision in the presence of any considerable degree of obstruction, though it be slight, is a dangerous procedure accompanied by a high mortality. A preliminary colostomy or the Mikulicz operation, where feasible, is a far safer and wiser procedure. Where there is no obstruction or marked dilatation of the proximal segment, the choice between the primary radical and the two-stage operation will depend upon many factors: the condition of the patient at the time of operation, whether he be fat or thin, the location and the mobility of the growth, etc., and the choice of the individual operator. It would seem from our series that primary radical excision in properly selected cases was the method of choice. Whether the anastomosis be lateral, end-to-side, end-to-end, or whether the Balfour modification of the end-to-end by the aid of a tube, etc., be done, are considerations that vary in the opinions of the different operators. There is, however, a marked tendency among some surgeons at the present time to show preference for the end-to-end anastomosis between the small and the large intestine as well as end-to-end anastomosis in the large intestine. The Mikulicz operation has a very important field, since it can be rapidly done and is a safer procedure in the hands of many surgeons with the added advantage of being applicable in acute ileus, and especially when the growth is located in the sigmoid.

An anastomosis around an inoperable growth will probably prolong life, is preferable and far more acceptable to the patient than a permanent colostomy, which should be deferred as long as possible in inoperable and obstructive conditions.

A CONTRIBUTION TO ECHINOCOCCUS DISEASE OF THE KIDNEY*

James I. Russell, M.D., and
Edward F. Kilbane, M.D.

IN reviewing the literature of echinococcus disease of the kidney and adding a case thereto, it is not our intention, nor is it within the scope of this paper, to discuss the zoological distribution, the life cycle, etc., of this very interesting little tapeworm (*Taenia echinococcus*).

With the exception of Nicaise's two very valuable contributions, namely, *Thèse de Paris*, 1904–1905, *Arch. gén. de chir.*, 1909, III, 453, the literature is very fragmentary and, for the most part, from those countries in which echinococcus disease is much more frequent than in ours. The contributions from the North American hemisphere have been very few indeed, and, for this reason, we have deemed it wise to call attention to the possible existence of this disease in the diagnosis of those unusual and obscure conditions met with from time to time in the region of the kidneys. Nicaise (*Arch. gén. de chir.*, 1909, III), collected 402 cases, but neither tabulates nor lists them by reference. Hence, we have tabulated and referenced, so far as possible, these cases, 43 in number, appearing in the literature since Nicaise, *Thèse de Paris*, 1904–1905, in which he has given a most extensive bibliography. Of the 402 cases collected by him, 216 were treated surgically, 169 of these by drainage, enucleation of the cyst or partial nephrectomy, with a mortality of 7.1 per cent. In the second group of 42 cases treated by nephrectomy, there was a mortality of 19 per cent. He advises the employment of the more conservative method and cautions against nephrectomy, since it is productive of so great a mortality. Kümmell, H., and Graff, H. (*Handb. d. prakt. Chir.*, 1914, IV), state that echinococcus cyst of the

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kidney is rare and that there are 36 cases in which operations have been performed, which statement we interpret to apply to the German Rhenish provinces. They believe the cysts never to be multiple, and that, in spite of the compression in the cyst, some renal tissue is always left. The only treatment considered is marsupialization, except in especially favorable cases which permit of a partial resection of the kidney followed by suture. They treated 1 case in this way, thereby shortening the convalescence.

While echinococcus cyst of the kidney may appear at almost any age, the youngest and the oldest patients that we have been able to find were three years and seventy-four years respectively. It is probably more frequent during middle life. It is more prevalent in females than in males and is said to attack the left kidney more frequently than the right. There is a wide variation among authors in the frequency in which echinococcus disease occurs in the kidney. Haynes states that it is 3.7 per cent, and that it is usually associated with echinococcus disease of other organs (*Ann. Surg.*, 1902, xxxvi). H. Vegas, and D. Cranwell, state that in 920 cases of echinococcus disease, it occurred 20 times in the kidney, or 2.1 per cent (*Centralbl. f. Chir.*, 1904, No. 3). Prat reports that in 471 cases of echinococcus disease, it occurred twice in the kidney (.42 per cent). (*Revista d. l. Hospitale*, Tome vi, No. 8, 1913.) Ribera states that in 117 cases of echinococcus disease, it occurred 7 times in the kidney (5.9 per cent).

The cyst may invade the whole kidney leaving no parenchyma, as in our case, or it may involve only a portion of the kidney, one pole or the other, or it may grow in the pararenal tissue only, compressing the kidney; furthermore, the cyst may or may not open into the kidney pelvis. The cyst is usually very adherent to the surrounding organs and the wall may be the seat of calcareous deposits. Upon its location, duration, size and involvement, the operative procedure necessarily depends. Echinococcus cyst has been reported in nearly all the different kidney conditions. Eberle and Celowski independently found it associated with floating kidney; Monad and Lance, independently, in hydronephrosis. Houzel did a nephrectomy for echinococcus

cyst in a solitary kidney, proved by autopsy. Juvara did a nephrectomy for hydatid of a left ectopic kidney. It has been associated with hydatid of the liver and other organs. Parlavecchio and Nicholich each report a case of hydatid cyst of the kidney rupturing into the bronchi and intestine with the discharge of daughter cysts through these ways as well as through the urethra. Hydatid cyst of the kidney is a slow-growing tumor extending over years and may present a varied degree of symptoms, or none. From symptomless tumors accidentally discovered in the course of examination, the picture changes through the varied stages of pain and discomfort in the lumbar region to the severe cases of renal colic, associated with hematuria or not, and with or without the expulsion of daughter cysts in the urine. These symptoms recur in attacks of greater or less severity from time to time. In those cases in which the cyst has opened into the renal pelvis with the expulsion of cysts or hooklets in the urine, the diagnosis is self-evident. On the other hand, when these symptoms are lacking, it is rarely possible to arrive at a correct diagnosis. The Weinberg complement-fixation test (*Ann. d. l'Inst. Pasteur*, 1909, No. 6) being positive, an associated eosinophilia with the presence of a tumor in the kidney region would point strongly to echinococcus disease of this organ; on the other hand, with a negative urine, cystoscopic and ureteral examination, with no palpable tumor, the eosinophilia and the positive Weinberg complement-fixation test (which is said to be present in two-thirds of the cases) is of but little assistance in localizing the hydatid even if it be present.

Welsh, Chapman and Storey (*Transactions Australian Med. Congress*, 1909) believe the negative results in the precipitin reaction are inconclusive; that positive results are conclusive of hydatid invasion and are of very considerable clinical value; aspiration is cautioned against as a diagnostic procedure, since it is not infrequently followed by hydatid intoxication and incurs a danger of inoculation to other tissues, etc. The condition has been mistaken for ovarian cyst, appendicitis, pregnancy, floating kidney, hydronephrosis, pyonephrosis, etc. The cyst not infrequently undergoes pyogenic infection with the added symptoms of

this condition. The disease is a surgical one and the ultimate result is necessarily prognosticated by the patient's condition, the extent of invasion, the surgical procedure pursued and the occurrence or not of postoperative hydatid intoxication.

F. Dévé (*Rev. d. chir.*, Tome XLIII, Nos. 5, 6, 7) deals fully with hydatid intoxication both from the medical aspect and from the postoperative point of view. Briefly, he divides surgical postoperative hydatid intoxication into three classes: First, *benign*—hydatid fever, urticaria, etc.; second, *grave*—fever, urticaria, collapse, syncope, etc.; third, *fatal*—high and rapid rise of temperature, collapse, embarrassed respiration with nervous manifestations and death.

Aspiration or puncture is an unwise procedure for obvious reasons; besides, hydatid intoxication being more frequent after it than in other surgical procedures, there is danger of transplanting the parasite into neighboring tissues and causing the cyst to undergo suppuration from an added pyogenic infection. Intravenous injection of salvarsan has met with but little success and it is apt to cause the cyst to undergo suppuration with the possibility of rupture and a fatal outcome. Enucleation of the cyst or partial nephrectomy, the method of choice, is applicable only in certain cases. Marsupialization and incision and drainage have the disadvantage of slow healing and the danger of secondary pyogenic infection. Bonamy (*Paris Chirurg.*, 1910, II) cites a case in which he marsupialized the sac and in which carcinoma developed two years later, the patient dying from hemorrhage. On the other hand, either one is a short, quick operation and attended with a low mortality. Nephrectomy may be a very difficult operation, as it was in our case. The cyst is usually very adherent to the surrounding tissue, especially anteriorly to the peritoneum and the intestines. The peritoneum is so closely adherent that it is difficult to deliver the kidney and cyst into the wound without entering the peritoneal cavity and there is the added danger of causing injury to the intestines. It has the great advantage of a short convalescence and is highly preferable to drainage in properly selected cases. Briefly, whether we shall do an enucleation, a partial nephrectomy, a marsupialization, a drainage or a nephrectomy, depends upon the conditions encountered

at the time of operation. Should postoperative hydatid intoxication supervene, Prat advises the administration of adrenalin chloride 1:1000, which he found to neutralize toxic doses administered to dogs.

History of Case (B8544). Italian male, aged forty-six years. Entered The Roosevelt Hospital October 20, 1916. Discharged December 16, 1916, with the following brief history: He is married, has two children living and well. Has had no previous acute illness, does not use alcohol, smokes very moderately, two or three pipes a day. Denies venereal infection. Six months ago he had an attack similar to the one for which he entered the hospital. Eight days before coming to the hospital, he had a chill and fever followed by pain and burning in the right kidney region. There was no nausea or vomiting and no urinary symptoms except that he thought the urine a little darker during the attack, but had noticed no blood. Upon questioning him further after operation, we elicited the fact that he had observed small grape-like cysts in his urine from which he could squeeze watery contents. Had we obtained this statement before operation, a correct diagnosis should have been made. The physical examination elicited slight tenderness over the right kidney; no mass could be felt. His fever reached 101° upon the first two evenings and then remained normal until after operation. White blood-cells, 9400; polymorphonuclears, 72 per cent; large lymphocytes, 12 per cent; small lymphocytes, 11 per cent; cosinophilia, 4 per cent; basophiles, 1 per cent. The x-ray findings were negative. The urine was normal except for a few pus cells.

Cystoscopic Examination. Bladder urine very turbid, the last portion by catheter being thick pus. Bladder mucosa markedly congested. Bladder tolerance very poor, the bladder holding only a small quantity of fluid, about 4 oz., and even this small amount caused intense straining and desire to urinate. Catheter passes to the left pelvis very easily. Flow of urine began immediately; normal as to rate and character of flow and clear in gross appearance. Catheter passes to right pelvis very readily. No flow of urine observed. Several catheters used, all with the same result. Fluid injected into the right pelvis to start the flow came back very turbid, but nothing else was obtained. Urine from the left kidney practically normal. Fluid from the right kidney contains large number of pus cells. Further examination to confirm finding on the right side advised (Oct. 23, 1913).

Findings exactly the same as on previous examination. No flow obtained from the right side except the return of the small amount of fluid injected to start siphonage. The pus in the urine, the congested bladder mucosa, the intolerant bladder, suggest the presence of an infected kidney on the right side. Kidney probably entirely destroyed. Left kidney performing entire renal function.

Operation (Oct. 28, 1916). By James I. Russell. Right nephrectomy through an oblique lumbar incision. The kidney, situated very high, was the seat of a large semifluctuating tumor with apparently very little, if any, kidney tissue left. It was quite adherent posteriorly and densely so anteriorly,

the peritoneum could not be stripped from it without entering the peritoneal cavity. After freeing it anteriorly, without injury to the intestine, the mass could not be delivered into the wound. An attempt to empty it through a suction cannula failed, due to the thickness of the contents of the cyst. It was necessary to divide the twelfth rib to deliver the kidney into the wound, in doing which the pleura was accidentally opened. The ureter, which was tremendously enlarged and thickened to the size of my thumb, was freed as as far as possible and divided, cauterized and ligated; the usual closure and drainage were established. Patient made a smooth and uninterrupted recovery, but now has a small hernia in the lower and anterior portion of his wound.

Upon removal, the kidney, much enlarged, measured 16 cm. by 13. About 3 in. of ureter, which is about 6 cm. in circumference, and very much thickened, was removed with the kidney. The kidney tissue had entirely disappeared and none was recognizable microscopically. The whole kidney was occupied by a large echinococcus cyst with daughter cysts. The cyst communicated with the pelvis.

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A NEW METHOD OF INTERPRETATION OF THE RENAL FUNCTION TEST MEAL*

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IN a previous paper[1] we discussed the renal functional test meal and the interpretation of renal function as judged by specific-gravity variation of the two-hour specimens and character of night urine, and offered clinical evidence purporting to illustrate the influence of several extrarenal factors† on the test-meal reaction. These extrarenal factors interfere considerably with the uniformity of response to the test meal by the same individual, at least upon viewing the responses in the manner heretofore suggested by Mosenthal. Subsequent to the publication of our study, Mosenthal[2] reported further studies in renal response to diets in which he felt obliged to revise his previous dicta as to evidences of normality and the significance of certain deviations therefrom, although still adhering to volume and specific gravity as the essential criteria of renal function. The nature and direction of his revision can be gleaned from an inspection of Table 1, which contains in parallel columns his earlier and later standards of normality.

The studies on which this report is based were completed previous to the publication of Mosenthal's later investigation, and were the outcome of an effort to circumvent the difficulties presented by his earlier definitions on interpretation of the test diet, and become, it appears to us, more effective in the light of his later report. We reserve for

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† By the phrase "extrarenal factors" in connection with reactions to the test diet, we refer to those influences upon renal excretion that occur independent of the stimulation supplied the kidney by the test diet and hence a variable influence not controlled by the test.

another time, however, the presentation of studies based on the added data supplied us in his more recent publication.

We felt satisfied that extrarenal influences on the reactions to the renal functional test diet operated chiefly through their effects on the supply of fluid to the kidney. We decided, therefore, to study the reactions chiefly in terms of the total solids eliminated, and some of the results of such studies we desire to make the subject of this report. The test meals used followed the outline by Mosenthal.[3] All the meals were served from a special diet kitchen conducted under the supervision of the pathological laboratory at The Roosevelt Hospital. The meals were served at 8 A.M., 12 M. and 5 P.M. Two-hour urine specimens were collected from 8 A.M. to 8 P.M., and the night specimen from 8 P.M. to 8 A.M. of the following day. Special care was taken to see that exactly three hours elapsed between the taking of the evening meal and the beginning of the collection of the night specimen.

TABLE 1

NORMAL STANDARDS FOR TEST MEAL FOR RENAL FUNCTION

		Later standard†		
	Earlier standard*	High diet	Low diet	Normal diet
Maximum specific gravity	1.018+	1.018+	1.020+	1.020+
Degree variation of sp. gr. usually	9+	9+	9+	No value
Sp. gr. of night urine	1.018+	Of no significance		
Volume c.c. of night urine	400 c.c. or less	750 c.c. or less		
N and NaCl per cent in night urine or highest per cent in any specimen.	1	Normal if 1 per cent or higher, not necessarily abnormal if less		

* Earlier standard: Mosenthal, H. O., and Lewis, D. S. *J. A. M. A.*, 1916, LXVII, 933.
† Later standard (see note 3).

It being, of course, rather impracticable to seek to determine the total urinary solids by any analytical method, we adopted the very simple yet fairly accurate method of calculating the total solids present from the specific gravity of the specimen. For accurate estimations it is quite essential that all the solids in the urinary specimens be in solution. To insure such solution, we followed the procedure of warming the specimen to about 40° C., at which temperature quite

all the urinary sediments readily went into solution with no danger of decomposition of nitrogenous solids. After allowing specimens to cool down to about 28° C., hydrometric readings were taken. The product of the last two figures of the specific gravity and the volume in cubic centimeters divided by 1000 and the quotient multiplied by the constant 2.3 as determined by Haeser, or 2.6 as estimated by Long,[1] gives approximately the grams of solids present in the given volume of urine. Being more concerned with ratios than with absolute quantities we have dispensed with the constant multiplier and so the figures used throughout this report as representing the solid content of specimens are the products of the last two figures of the specific gravity and volume in cubic centimeters of the specimens and should be multiplied by the constant to give grams of solids.

In the study of the test-meal reaction we have concerned ourselves with several features of the eliminated urinary solids.

Firstly: The total twenty-four-hour solids eliminated; this in the average individual without definite renal insufficiency has under the stimulus of the renal test diet approximated 25.[5]

With definite renal insufficiency there have appeared decided reductions in the quantity of urinary solids for the twenty-four-hour period. Although this has been the general tendency, the total daily output for many individuals of the normal group has fallen well within the limits of the nephritic group and the variations for the same individual have in many instances been quite marked. This was to be expected considering the many factors that enter into the determination of the total twenty-four-hour urinary solids for any particular day; i. e., the nitrogen salt-and-water balance of the body on the day of the test, the degree of stimulating power in the test diet for the particular kidneys tested, the perfect functioning of the gastrointestinal tract assuring the passage of the stimulatory food to the blood stream, sufficient supply of water for the elimination of the solids and the several secondary factors that in turn affect such a supply. The item of the total solid output for the twenty-four hours has, therefore, little significance as an index of renal

efficiency except in cases where it deviates very considerably from the normal.

Secondly: The ratio of the quantity of solids eliminated from 8 A.M. to 8 P.M. to that eliminated from 8 P.M. to 8 A.M. the following morning; the ratio of the day to the night output of urinary solids. This ratio we have designated Factor 1.

In view of the fact that early renal involvement very often manifests itself as a delay in the excretion of metabolites, it is quite conceivable that such a ratio might disclose such a delay long before the excretory function has been impaired to the point of actual retention of metabolites. Furthermore, a separation of the renal stimulatory period—the period of food intake and greatest activity of the integral organism, from the nonstimulatory period—the period of minimal body activity, best serves to restrict the renal activity of the latter period to responses to stimulation by the circulating residual metabolites. Such a restriction is naturally a desideratum, for under these conditions the urinary output of the night period supplies a unit serviceable in arriving at a close and fair index of the rate of excretion of the metabolites formed from the food ingested during the day.

For proper emphasis of the cogent concept underlying this day to night ratio one might state the idea thus: the day to night ratio of eliminated solids represents the quantum of excretory substances eliminated during the day, the said quantum expressed in units of nocturnal residual metabolites (solids of night period).

Thirdly: A modification of Factor 1, the incorporation of the element of actual total twenty-four-hour solids eliminated. If we sought to establish indices of renal function in terms of the rate of elimination of metabolites, such a rate would have to be expressed with reference to some unit of quantity.

With all other things equal, the more solids the kidney is called upon to excrete, the more time it needs for such elimination; and the kidney cannot be expected to maintain the same ratio of day to night elimination, as the total twenty-four-hour output fluctuates.

This statement necessarily demands more than the mere expression of it for its acceptance. We might hasten to add that we are not aware of any physiologic principle of renal activity that compels this conclusion; nor naturally of any principle that forbids it. In the absence of guiding generalizations we must fall back upon our data for substantiation. We find on examination of our data for the normal cases the existence of a negative correlation between the magnitudes expressive of Factor I and of the total twenty-four-hour solids. This is to say that the mutual relationship between these two characteristics of the reaction is such that, in general tendency, the higher, numerically, Factor I, the lower the total twenty-four-hour solids. Our data, therefore, permit of the implication made in the preceding paragraph.

We have, therefore, taken 25,[5] which appears to be about the average total solid output on a full diet in the average normal individual, as the unit of quantity. We have in each case multiplied Factor I by the ratio $\frac{\text{total 24-hr. solids}}{25}$. The resulting product we have designated Factor II. To the extent to which this latter ratio (total twenty-four-hour solids divided by 25) approximates unity, Factor II will numerically approximate Factor I, falling below it as the ratio falls below one, exceeding it as the ratio increases above one. Factor II, then, involves the added element of the absolute quantity of solids excreted.

Fourthly: A further introduction of the element of concentration of urinary solids.

The concentration of the eliminated solids is a feature of kidney activity long shown to be significant in the study of renal function. Factor II, has, therefore, been multiplied by the ratio $\frac{1500}{\text{total volume 24 hrs.}}$ (1500 c.c. being selected as an acceptable [upper range] average daily output). This product has been called Factor III.*

* That Factor III is equivalent to Factor I, multiplied by the sp. gr. of the total twenty-four-hour specimen, times a constant, can be seen from the

So then, as the total volume exceeds 1500 c.c., Factor III becomes numerically smaller than Factor II, and as it falls below 1500 c.c. it increases in like ratio above Factor II.

It may be emphasized at this point that with the introduction of these several "factors" we are not seeking to express or establish any mathematical law of kidney excretion, nor are we desirous of adorning the physiology of kidney function with the cloak of mystic numbers. Primarily, our purpose is to study the rate of excretion of urinary solids. This rate we have chosen to estimate in terms of the ratio of the solids excreted during the day to that excreted at night. Inasmuch as such a ratio would be affected by the total quantity of solids excreted as well as by the total volume of fluid, and inasmuch as it was necessary, if we desired to secure comparable ratios, that constants be introduced about which these ratios were to swing, Factors II and III were introduced. We arbitrarily and empirically selected 25^5 as the total solid constant and 1500 as the total volume constant, both of which figures fairly well represent the average output respectively of solids and fluids. Since with the increase of the total solid output the day to night ratio tends on the whole to become numerically smaller, we introduced the solid constant in a manner to counterbalance this reduction;

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following:

$$\text{Factor I} = \frac{\text{Sp. gr.} \times \text{vol. (of day spec.)}}{\text{Sp. gr.} \times \text{vol. (of night spec.)}}$$

$$\text{Factor II} = \frac{\text{Factor I} \times \text{sp. gr.} \times \text{vol. (of 24-hr. spec.)}}{25}$$

$$\text{Factor III} = \text{Factor II} \times \frac{1500}{\text{Vol. (of 24-hr. spec.)}}$$

$$= \frac{\text{Factor I} \times \text{sp. gr.} \times \text{Vol.(of 24-hr. spec.)}}{25} \times \frac{1500}{\text{Vol.(of 24-hr. spec.)}}$$

$$= \text{Factor I} \times \text{sp. gr. (24-hr. spec.)} \times \underbrace{\frac{1500}{25}}_{\text{[constant]}}$$

The constant $\frac{1500}{25}$ is a ration expressive of a function of a concentration since the 1500 represents volume and the twenty-five solids contained therein. Factor III, therefore, falls back for its derivation on Factor I, and results from introducing into this latter "factor" the element of concentration of solids in the urine. Thus, both Factors II and III are derived with equal directness from Factor I.

by Factor II increasing above Factor I, in direct proportion to the increase of total twenty-four-hour solids over 25.[5] Furthermore, since a diminution in the amount of fluid supplied to the kidney has a tendency to hold back urinary solids as well, reducing the total solid output and likewise delaying the rate of excretion of solids, the volume constant* was introduced in a fashion to offset this interference by Factor III increasing numerically above Factor II in propor-

TABLE II

NON-NEPHRITIC CASES

Case	Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids*	Factor		
			Volume	Sp. gr.	N. conc. per cent			I	II	III
1	1.020	10	210	1.018	0.74	9.43	27.9	6.40	9.60	7.99
2	1.020	6	225	1.022	0.59	11.3	28.47	4.50	5.10	4.60
3	1.023	10	225	1.017	1.25	9.7	24.67	5.45	5.40	5.70
4	1.016	10	133	1.020	0.90	7.83	20.45	6.70	5.50	5.05
5	1.031	16	208	1.022	1.69	15.67	29.17	3.96	4.60	5.60
6	1.022	10	212	1.030	1.70	13.2	31.2	3.91	4.87	4.47
7	1.025	14	255	1.027	1.21	9.3	30.5	3.36	4.76	3.78
8	1.032	18	320	1.028	1.20	10.00	33.58	2.75	3.80	4.10
9	1.017	6	218	1.023	0 70	8.47	22.7	3.55	3.23	3.15
10	1.024	15	170	1.030	1.43	7.62	20.27	2.98	2.42	2.80
11	1.030	23	165	1.035	1.81	9.30	23.1	3.02	2.80	3.41
12	1.025	16	185	1.028	1.28	8.50	21.1	3.06	2.58	3.00
13	1.026	15	281	1.024	1.38	11.5	22.45	2.32	2.08	2.65
14	1.022	12	300	1.028	1.48	10.0	26.11	2.10	2.20	2.31
15	1.017	8	380	1.017	0.68	7.89	23.38	2.45	2.20	2.12
16	1.026	16	220	1.026	1.24	8.39	20.50	2.60	2.08	2.67
17	1.025	15	236	1.025	1.58	12.13	24.52	3.15	3.10	3.18
18	1.022	13	224	1.026	1.27	9.36	25.48	3.37	3.42	2.92
19	1.030	10	164	1.031	1.97	13.24	21.77	3.22	2.80	4.53
20	1.021	8	209	1.028	1.53	9.27	23.91	3.08	3.07	3.76
21	1.020	10	265	1.016	0.72	8.59	19.77	3.65	2.90	2.48
22	1.034	12	270	1.030	1.49	10.88	24.83	2.06	2.05	3.31
23	1.018	8	235	1.027	1.26	10.21	31.35	3.94	4.92	3.64
24	1.030	18	564	1.018	1.02	13.46	33.90	2.38	3.20	2.46
25	1.022	10	340	1.026	1.09	10.79	33.06	2.77	3.61	2.91

*The numerical values for the total solids here given represent the estimated solids divided by the constant multipliers 2.3 or 2.6, the constants involved in estimating urinary solids from a knowledge of the volume and specific gravity of a specimen.

tion to the reduction of the twenty-four hour volume below 1500 c.c. In a word, our desire has been to secure numerical ratios representing the rate of excretion of urinary

*See footnote, page 307.

solids, the said ratios being corrected for the total quantity of solids and fluids* eliminated in the twenty-four hours and such corrections have been introduced in the form of Factors II and III. Just what such an attempt secured we submit below.

In addition to the estimation of the three "factors" as explained above, we have included in the tabulations given the significant data of each test-diet reaction sufficient to permit of their interpretation in the terms adopted by Mosenthal. The maximum specific gravity of the two-hour specimens, the amount of night volume, its specific gravity and its nitrogen concentration supply the data upon which his interpretation of the reaction is based. In addition, the tables contain the estimated total solids and total nitrogen determinations.

In Tables II and III we have tabulated the test-meal reaction of 50 unselected non-nephritic cases. In Table II are assembled those all of whose "factors" numerically equal or exceed two. In Table III are listed those in which at least one factor equaled or exceeded two. In the reactions of Table II, we find that the variations in specific gravity of the two-hour specimens are very good, the night urine tends to remain below 400 c.c. with a specific gravity usually well above 1.018 and a nitrogen concentration about 1 per cent; all these features of the reaction early looked on by Mosenthal as indicative of the certainly normal response. In Table III, the reactions also quite well approximate the specifications for the normal reactions as laid down by him. Here, however, several striking deviations from the average normal reactions appear; increase of night volume above 400 c.c. (Cases 4, 8, 9, 21); reduction of specific gravity of night specimen below 1.018 (Cases 4 and 15). That extra-renal factors can and do operate in normal individuals to produce these deviations from the norm we have demonstrated in another report[1] and appreciation of this has led Mosenthal[2] to revise his original standards of normality.

From a perusal of Table II, then, it appears that in normal individuals with definitely normal test-meal reactions the ratio of solids passed during the day twelve hours to that passed during the night twelve hours is at least 2:1; and

*See footnote, page 307.

further, that the total solids are sufficient in amount and the total volume of urine for the day sufficiently low (i. e., concentration of solids sufficiently high) to keep Factors II and III as well, numerically above two. *Or, to express it in terms of clinical*

TABLE III

NON-NEPHRITIC CASES

Case	Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids*	Factor		
			Volume	Sp. gr.	N. conc. per cent			I	II	III
1	1.022	6	405	1.020	1.28	13.3	23.69	1.92	1.82	2.22
2	1.023	6	315	1.025	1.46	9.7	22.38	1.85	1.66	2.33
3	1.025	17	470	1.018	0.87	10.88	28.05	2.32	2.60	1.95
4	1.024	14	600	1.015	0.74	10.6	26.94	1.99	2.14	1.71
5	1.029	4	400	1.027	1.27	10.2	26.75	1.48	1.58	2.43
6	1.021	13	307	1.024	1.29	8.8	22.8	2.08	1.90	1.82
7	1.020	8	412	1.018	0.83	9.0	23.2	2.12	1.97	1.97
8	1.031	3	575	1.018	0.99	12.40	25.18	1.44	1.48	2.02
9	1.014	8	520	1.020	0.85	11.28	31.6	2.03	2.56	1.54
10	1.030	10	300	1.020	1.26	8.30	16.48	1.75	1.45	2.43
11	1.030	15	400	1.016	0.85	8.58	20.86	2.26	1.88	2.10
12	1.020	6	325	1.020	1.07	8.26	20.48	2.16	1.77	2.30
13	1.031	1	170	1.031	2.42	10.93	14.54	1.74	1.01	3.20
14	1.020	11	200	1.021	0.68	9.87	13.76	2.28	1.25	1.98
15	1.022	10	450	1.014	0.67	6.46	20.19	2.20	1.76	2.28
16	1.029	4	325	1.029	1.19	8.39	23.43	1.47	1.38	2.45
17	1.022	4	265	1.025	1.48	8.55	18.08	1.73	1.25	2.23
18	1.016	5	180	1.024	1.17	6.20	17.93	3.16	2.28	1.86
19	1.014	7	370	1.016	0.76	6.95	18.80	2.17	1.60	1.58
20	1.026	12	330	1.026	1.19	9.20	23.60	1.75	1.65	2.35
21	1.025	10	790	1.017	0.70	14.9	34.68	1.59	2.21	1.74
22	1.033	5	342	1.031	1.50	11.30	24.06	1.27	1.22	2.30
23	1.023	14	490	1.020	0.91	11.2	28.74	1.94	2.23	1.82
24	1.020	11	214	1.020	1.05	6.91	17.62	2.60	1.83	2.20
25	1.024	20	185	1.032	1.42	7.23	17.22	1.92	1.32	2 02

* The numerical values for the total solids here given represent the estimated solids divided by the constant multipliers 2.3 or 2.6, the constants involved in estimating urinary solids from a knowledge of the volume and specific gravity of a specimen.

equivalents, the definitely normal reaction to the renal function test diet is an excretion of at least twice the amount of solids during the day as night with a total solid elimination of about 25[5] and a total twenty-four-hour volume of urine of not over 1500 c.c.

In Table III the responses to the test meal by normal individuals have been, on the whole, slightly poorer, and

TABLE IV

CARDIOVASCULAR CASES

	Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids	Factor			Diagnosis
			Volume	Sp. gr.	N. conc. per cent			I	II	III	
1	1.015	6	870	1.011	0.56	10.3	18.57	0.94	0.70	0.60	Chronic endocarditis, arteriosclerosis, myocarditis
2	1.017	2	202	1.020	1.14	5.04	7.8	0.78	0.25	0.90	Chronic cardiac insufficiency, myocarditis
3	1.029	6	570	1.025	1.01	11.9	25.35	0.95	0.96	1.36	Hypertensive cardiovascular disease
4	1.021	10	332	1.021	0.98	6.28	14.43	1.01	0.61	1.25	Hypertensive cardiovascular disease
5	1.025	7	198	1.024	....	.....	10.7	1.27	0.55	1.70	Chronic cardiac insufficiency, syphilis
6	1.024	6	601	1.018	0.52	7.72	25.20	1.41	1.43	1.48	Chronic cardiac insufficiency
7	1.023	2	1210	1.015	0.61	15.2	25.65	0.96	0.99	0.74	Cardiac insufficiency, eliminating edema
8	1.022	10	890	1.010	0.32	6.44	17.76	0.99	0.70	0.70	Chronic cardiac insufficiency, chronic endocarditis
9	1.028	8	300	1.025	1.31	7.37	12.57	0.68	0.34	0.97	Chronic cardiac decompensation
10	1.022	7	300	1.020	0.83	5.32	12.07	1.01	0.49	1.18	Chronic myocarditis
11	1.020	10	632	1.018	0.61	7.43	22.06	0.93	0.83	0.92	Cardiac insufficiency, mitral stenosis, auricular fibrillation
12	1.020	5	397	1.018	0.77	8.88	17.57	1.46	1.03	1.56	Aortic aneurysm
13	1.021	9	560	1.016	0.58	9.38	21.35	1.38	1.18	1.37	Aortic aneurysm

though all the "factors" have not reached two, at least one of them has, and those "factors" that have failed to reach two are considerably above one. It would appear, therefore, that in normal individuals, even where extrarenal elements might have entered to prevent a strictly normal test-meal reaction, the introduction of the several salient features of renal response in the manner attempted has succeeded in bringing at least one "factor" numerically above two. Thus this procedure for estimating the result of the test-meal reaction seems able to correct for the interfering influences upon the reaction consequent upon responses of the kidney to stimuli from uncontrolled sources, for with oliguria there is compensatory increase in concentration of solids, and with polyuria an approximately equivalent reduction in solid concentration.

In Tables IV, V and VI, are given the findings in cardiovascular, cardionephritic and nephritic cases.

Cardiovascular Cases. In the patients with well-marked cardiovascular disease, as was the case with the patients here listed, the nutrition of the kidney is markedly interfered with and the renal function similarly disturbed. Where through kidney congestion and circulatory embarrassment there is interference with the elimination of water, as in Cases 2, 4, 5, 9 and 10 (Table IV), the excretion of solids is much delayed and the total amount of solids eliminated in the twenty-four hours is well below normal. Nitrogen excretion is least hampered, which fact in conjunction with the oliguria results in the excretion of nitrogen in good concentration and with a night specimen well below 400 c.c. However, in cases in which apparently arteriosclerotic changes in the kidney predominate, there is frequently definite interference with the power for elimination of nitrogen in good concentration, in which cases the reactions to the test diet approximate those of interstitial nephritis. Under these conditions the night specimens are increased in volume and nitrogen concentration is low (Cases 1 and 8). Where beginning cardiac compensation is evidencing itself by the elimination of edema, the total solids and fluids excreted are much increased, but the rate of elimination of the solids as expressed in terms of the ratio of the day to night solids is

well below that in normal cases (Case 7). Thus, be the test-meal reaction one of oliguria from renal congestion, or that of the arteriosclerotic kidney simulating the reaction of interstitial nephritis or that of polyuria from the elimination of edema, the rate of solid excretion as estimated in the fashion we have herein attempted is very considerably reduced below that found in our normal cases. The numerical values of all three "factors" are well below two, all tending, on the whole, to border about and usually below one.

Cardionephritic and Nephritic Cases. Be the functional reaction of the kidney more indicative of the circulatory disturbance in the cardionephritic or of his renal lesion—be the renal condition one interfering primarily with the salt-and-water or with the nitrogen elimination, the rate of excretion of the urinary solids is much delayed and the total amount of solids, on the whole, definitely reduced below that found in normal individuals. Usually all three "factors" as calculated fall numerically well below two, a high percentage of them dropping below one. The reactions, likewise, viewed in the terms of specific gravity variation of the two-hour specimens and character of night urine, correspond with those found and described as indicative of renal insufficiency. With renal involvements, then, there appears a definite delay in the excretion of urinary solids—a definite increase relatively and at times absolutely in the quantity of solids excreted at night.

In Tables VII and VIII, we have grouped reactions to the test diet given to the same individual on two, three or more days, many of the tests in the same individual being given on consecutive days. It appears therefrom that the results expressed in terms of the rate of solid excretion by means of the three "factors" show very acceptable consistency for the same individual. In the group of normal cases, the same individual in several test-meal reactions, be the reaction characterized by total oliguria with high concentration of all specimens (S 299), or by high night volume with reduced specific gravity (S 297, O 320), or by the nitrogen concentration in the night specimens considerably above 1 per cent or below it (O 320 or O 321), supplied "factors"

TABLE V

CARDIONEPHRITIC CASES

	Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids	Factor			Diagnosis
			Volume	Sp. gr.	N. conc. per cent			I	II	III	
1	1.029	4	350	1.028	1.77	11.8	19.46	0.98	0.76	1.63	Chronic cardiac insufficiency, chronic nephritis
2	1.031	10	116	1.031	1.68	5.48	11.35	2.16	0.98	3.78	Chronic hypertensive cardiovascular, chronic nephritis
3	1.025	7	634	1.021	0.78	10.1	27.7	1.09	1.21	1.34	Arteriosclerosis, cardiac insufficiency, chronic diffuse nephritis
4	1.017	3	800	1.015	0.61	9.68	20.45	0.70	0.57	0.65	Cardiovascular disease, diffuse nephritis
5	1.016	6	233	1.016	0.84	4.10	7.40	0.98	0.30	0.85	Chronic cardiac insufficiency, diffuse nephritis
6	1.012	3	1014	1.000	0.39	8.97	19.9	1.19	0.95	0.68	Cardiac decompensation, chronic interstitial nephritis
7	1.021	2	212	1.023	1.14	5.86	13.07	1.67	0.87	2.14	Chronic cardiovascular disease, chronic diffuse nephritis
8	1.010	4	1056	1.009	0.28	7.28	18.67	0.97	0.72	0.49	Chronic cardiac insufficiency, chronic diffuse nephritis
9	1.014	4	535	1.012	0.55	5.72	11.95	0.86	0.41	0.62	Aortic insufficiency, chronic diffuse nephritis
10	1.013	2	725	1.010	1.25	14.67	19.50	1.56	1.21	1.10	Cardiovascular disease, chronic diffuse nephritis
11	1.018	8	875	1.008	0.32	5.08	13.87	0.98	0.54	0.58	Chronic endocarditis, arteriosclerosis, chronic diffuse nephritis
12	1.011	1	870	1.010	....	6.15	15.71	0.81	0.54	0.40	Chronic endocarditis, arteriosclerosis, chronic diffuse nephritis
13	1.020	13	615	1.017	0.55	7.18	20.17	0.93	0.75	0.72	Chronic cardiac insufficiency, chronic glomerulonephritis
14	1.020	10	740	1.020	0.58	9.0	27.21	0.84	0.92	0.79	Chronic cardiac insufficiency, chronic nephritis
15	1.025	6	460	1.020	0.60	5.47	18.14	0.97	0.71	1.22	Chronic cardiac insufficiency, chronic glomerulonephritis
16	1.010	4	1056	1.009	0.28	7.28	18.67	0.97	0.72	0.49	Chronic cardiac insufficiency, chronic diffuse nephritis
17	1.016	3	570	1.014	0.61	7.90	15.47	0.93	0.67	0.78	Aortic insufficiency, chronic diffuse nephritis
18	1.014	1	481	1.012	0.42	4.88	14.52	1.52	0.88	1.18	Chronic endocarditis, chronic diffuse nephritis
19	1.012	2	710	1.010	0.41	5.69	14.87	1.09	0.67	0.70	Chronic endocarditis, chronic diffuse nephritis
20	1.020	12	1450	1.010	0.28	7.93	28.38	0.96	1.09	0.55	Chronic endocarditis, chronic cardiac insufficiency

TABLE VI

NEPHRITIC CASES

	Maximum sp. gr.	Maximum sp. gr. Variation	Night urine			Total N. gm.	Total 24-hr. solids	Factor			Diagnosis
			Volume	Sp. gr.	N. conc. per cent			I	II	III	
1	1.021	8	615	1.017	0.79	13.6	24.77	1.38	1.36	1.39	Chronic interstitial nephritis
2	1.015	2	1185	1.012	0.41	10.74	33.38	1.35	1.80	1.05	Chronic interstitial nephritis
3	1.022	4	390	1.018	....	6.8	14.83	1.12	0.67	1.27	Chronic parenchymatous nephritis
4	1.018	8	1336	1.014	0.38	10.78	40.32	1.17	1.89	0.96	Chronic interstitial nephritis
5	1.017	4	515	1.016	0.61	6.0	18.38	0.88	0.64	0.73	Chronic interstitial nephritis
6	1.013	2	914	1.012	0.76	13.9	22.56	1.00	0.90	0.73	Chronic interstitial nephritis
7	1.020	8	460	1.025	0.44	4.86	10.38	0.69	0.53	0.73	Chronic interstitial nephritis
8	1.023	5	460	1.020	0.97	9.11	10.49	1.11	0.87	1.30	Chronic diffuse nephritis
9	1.016	4	700	1.011	0.33	4.7	15.87	1.06	0.68	0.80	Chronic interstitial nephritis
10	1.020	13	995	1.011	0.44	8.16	17.93	0.65	0.47	0.46	Chronic glomerulonephritis
11	1.030	12	888	1.010	0.46	8.4	18.0	1.03	0.75	0.83	Chronic interstitial nephritis
12	1.019	2	625	1.020	1.10	14.0	23.88	0.91	0.87	1.05	Chronic diffuse nephritis
13	1.029	22	814	1.012	0.58	9.8	22.1	1.20	1.11	0.88	Chronic diffuse nephritis
14	1.015	12	810	1.011	0.47	9.1	18.43	1.07	0.79	0.60	Chronic diffuse nephritis
15	1.028	15	1020	1.012	0.43	7.44	10.93	0.63	0.50	0.50	Chronic glomerulonephritis
16	1.017	3	700	1.016	0.62	8.92	22.79	1.03	0.94	0.80	Subacute glomerulonephritis
17	1.009	1	832	1.009	0.40	5.6	11.80	0.59	0.28	0.32	Chronic interstitial nephritis
18	1.029	15	899	1.010	0.67	10.1	17.53	0.95	0.67	0.79	Chronic interstitial nephritis
19	1.024	7	760	1.014	0.90	11.46	18.56	0.74	0.48	0.64	Chronic interstitial nephritis
20	1.028	2	590	1.020	1.2	10.9	19.01	0.61	0.46	0.81	Chronic interstitial nephritis
21	1.025	6	670	1.017	0.58	8.8	22.93	1.01	0.93	1.16	Chronic interstitial nephritis

one of which was numerically at least equal to two. So here too, it likewise appears that for the same non-nephritic individual on repeated examinations, even though successive reactions significantly vary in character of night specimen or two hourly specimens (S 296 and S 297—O 320 and O 321) the "ratio-factor" and its "corrective factors" still produce

TABLE VII

REPEATED TEST MEALS IN NON-NEPHRITIC INDIVIDUALS

		Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids	Factor		
				Volume	Sp. gr.	N. conc. per cent			I	II	III
S 207	12/ 6/16	1.022	10	340	1.026	1.09	10.79	33.06	2.77	3.61	2.91
S 294	2/ 5/17	1.023	7	540	1.018	....	.....	30.79	2.18	2.68	2.54
S 296	2/ 6/17	1.025	9	380	1.024	0.72	11.3	30 29	2.31	2.80	2.98
S 297	2/ 7/17	1.026	11	610	1.016	1.1	18.8	32.5	2.33	3.02	2.68
S 298	2/ 8/17	1.027	4	325	1.025	0.77	7.30	25.2	2.09	2.08	2.94
S 299	2/ 9/17	1.029	4	400	1.027	1.27	10.2	26.7	1.48	1.58	2.43
B 313	2/13/17	1.031	11	303	1.029	1.20	10.5	21.41	2.31	1.98	2.54
B 314	2/14/17	1.030	4	276	1.031	1.40	10.0	25.2	1.95	1.96	3.44
B 315	2/15/17	1.033	5	342	1.031	1.50	11.3	24.6	1.27	1.22	2.30
O 318	2/13/17	1.020	5	630	1.019	0.80	14.5	44.82	2.74	4.90	2.82
O 319	2/14/17	1.027	4	280	1.029	1.70	16.8	29.35	2.61	3.06	4.50
O 320	2/15/17	1.025	10	790	1.016	0.70	14.9	34.68	1.59	2.21	1.74
O 321	2/16/17	1.029	9	290	1.029	1.92	14.80	25.06	1.98	1.99	3.10
D 346	3/ 5/17	1.025	18	315	1.023	1.10	7.8	21.55	1.97	1.69	1.86
D 347	3/ 6/17	1.021	14	210	1.027	1.20	7.7	19.67	2.47	1.94	2.01
D 374	3/20/17	1.019	13	375	1.019	0.93	8.8	19.40	1.72	1.33	1.43
D 375	3/21/17	1.020	16	320	1.022	1.15	9.4	18.88	1.68	1.26	1.33
D 376	3/22/17	1.023	19	285	1.025	1.3	9.2	18.48	1.59	1.17	1.33
N 258*	1/24/17	1.029	3	500	1.025	....	.....	29.57	1.36	1.58	2.10
N 263*	1/26/17	1.023	10	340	1.018	....	.....	17.62	1.92	1.35	2.60
E 276*	1/31/17	1.023	15	550	1.010	....	.....	20.27	2.68	2.18	2.32
E 285*	1/28/17	1.033	10	212	1.024	....	.....	23.16	2.48	2.28	3.88

* No regular test meal; subjects on their ordinary diets.

a numerical product of at least two in one of the three factors. It is to be noted, too, that such was the case in individuals who were fed no special diets. Subjects N and E partook of their customary diets. In subject E's reactions

is to be observed the marked variation in the character of the night specimens of his two test meals: in one an increased night volume with a very low specific gravity and in the other a scanty night volume with a high specific gravity, and this with no appreciable difference in both test-meal reactions when considered in terms of the rate of excretion of urinary solids. Subject D succeeds but once in five test meals in securing "factors" numerically above two. She reacts rather constantly below the normal so far as the rate of urinary solids excretion is concerned; although her reactions, as viewed from the character of the volume and specific gravity of the day and night specimens, are consistently normal. We deem it somewhat premature to attempt to discuss further at this time any disagreement

TABLE VIII

REPEATED TEST MEALS IN NEPHRITIC INDIVIDUALS

		Maximum sp. gr.	Maximum sp. gr. variation	Night urine			Total N. gm.	Total 24-hr. solids	Factor		
				Volume	Sp. gr.	N. conc. 7 per cent			I	II	III
O 352	3/ 5/17	1.022	4	540	1.013	0.54	6.0	16.1	1.29	0.83	1.24
O 362	3/12/17	1.022	11	1101	1.009	0.26	5.8	21.8	1.14	0.97	0.80
O 363	3/13/17	1.022	5	870	1.011	0.36	5.4	17.03	0.78	0.58	0.20
O 366	.....	1.024	6	1085	1.007	....	.....	16.01	1.10	0.71	0.71
L 343	2/28/17	1.029	15	899	1.010	0.67	10.1	17.53	0.95	0.67	0.79
L 344	3/ 1/17	1.024	7	760	1.014	0.90	11.4	18.56	0.74	0.48	0.64
L 345	3/ 2/17	1.028	2	590	1.020	1.2	10.9	19.01	0.61	0.48	0.85
T 65	5/20/16	1.020	13	615	1.017	0.55	7.18	20.17	0.93	0.75	0.72
T 67	5/27/16	1.024	10	430	1.014	0.40	4.25	17.44	1.91	1.31	1.89
T 81	6/15/16	1.025	6	460	1.020	0.60	5.47	18.14	0.97	0.71	1.22
T 127	9/ 1/17	1.019	9	750	1.011	0.38	7.16	16.14	0.96	0.62	0.73
T 134	9/26/17	1.017	7	725	1.014	0.50	8.48	23.8	1.37	1.31	1.11
T 158	10/30/16	1.020	10	725	1.016	0.50	7.32	22.48	0.94	0.84	0.82
F 177	11/11/16	1.028	15	1020	1.012	0.43	7.44	19.93	0.63	0.50	0.50
F 186	11/18/16	1.020	13	995	1.011	0.44	8.16	17.93	0.65	0.47	0.46
F 199	11/28/16	1.018	8	1250	1.012	0.62	11.07	26.09	0.74	0.77	0.57
H 30	4/10/16	1.013	2	940	1.012	0.76	13.9	22.56	1.0	0.90	0.76
H 40	4/21/16	1.015	2	1185	1.012	0.41	10.74	33.38	1.35	1.80	1.05
H 49	5/ 3/16	1.010	1	970	1.010	0.39	9.02	24.7	1.55	1.53	0.92

in findings in the same individual by the two methods of test-meal interpretation. Sufficient for our present purpose is the observation that the rate of solid excretion method tends, at least, to be consistent with itself. Likewise, for the nephritic cases a similarly persistent constancy in reaction by the same individual manifests itself. As in the table of the nephritic groups above outlined, the "factors" tend to amount numerically to about, and, in greatest frequency, to below, one.

SUMMARY AND CONCLUSIONS

In a study of over 300 renal function test meals we have been impressed with the operation of extrarenal influences on the reaction, which in many cases interfered with the reliability of interpretations of the findings expressed in terms of the specific gravity variation of the two-hour specimens and character of the night urine. We endeavored to circumvent this interference, which, we suspected because of an earlier study was due to extraneous factors influencing the fluid supply to the kidney, by attempting to translate the renal function test-meal findings into terms of the urinary solids eliminated. The solids were estimated from the specific gravity and volume of the specimens and the following features of the excreted solids studied:

1. The total twenty-four-hour estimated urinary solids. This amounted on the average in normal cases to about 25 (this figure to be multiplied by constant 2.3 or 2.6 to secure in gm. the absolute amount of solids present.) In renal, cardiorenal and cardiac decompensation cases the urinary solids eliminated during the twenty-four hours usually fell well below this figure.

2. The rate of excretion of urinary solids expressed in terms of the ratio of the solids eliminated during the day to that of the night. To this ratio was applied the designation Factor 1.

3. The introduction of corrective checks upon Factor 1 for the absolute twenty-four-hour solids and volume eliminated, and in a manner to allow for a delay in rate of solid excretion consequent upon an increase in total solid output or reduction in amount of fluid excreted, thus permitting of compari-

sons between the numerical findings expressive of the rate of excretion in all our reactions. These checks are introduced as Factors II and III.

$$\text{Factor II equaling Factor I} \times \frac{\text{total 24-hr. solids}}{25}$$

$$\text{Factor III equaling Factor II} \times \frac{1500}{\text{total 24-hr. volume}}$$

Application of this method of interpretation showed that distinctly normal persons, with the test meal used, excrete at least twice as much of urinary solids during the day as during the night with a total twenty-four-hour solid elimination in the neighborhood of 25[5] and a total volume of about 1500 c.c. so that all Factors, I, II and III, produce the numerical equivalent of at least two.

In most cases in which influences might have entered to interfere with a normal response to the test meal, the corrective factors apparently operated to produce at least one "factor" numerically equal to two.

For kidneys with defective function, either by virtue of renal, cardiac or cardiovascular disease, there is evidenced both a reduction in the total solids excreted in twenty-four hours and a marked delay in the rate of excretion as estimated in terms of the ratio of day-to-night elimination of urinary solids. Hence, in these cases all three "factors" of the test-meal reaction tend to be numerically well below two; ranging, as a rule, about one as a mean.

This method of estimating the results of the renal function test meal presents as sharp a differentiation between the normal and subnormal functioning kidney as does the method based on a study of the specific gravity variation of the two-hour specimen and character of night urine.

It further appears to disclose greater constancy in reaction by the same individual, particularly in persons with normal or only slightly diseased kidneys, than does the former method.

This method obviates the need for collecting urinary specimens at exactly two-hour intervals.

Where urinary specimens have been collected in two hourly periods during the day, the results of the test can be judged

by both methods of interpretation as we have been able to do with all our cases.

The essential procedures in securing acceptable data for estimating the rate of solid excretion are: (*a*) patient to abstain from food or drink between meals; (*b*) heaviest meal to be taken at noon, and (*c*) three hours be permitted to elapse after the evening meal before beginning collection of the night specimen.

It was on the basis of this procedure with our test meals that the data above submitted were obtained.

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METHODS AND RESULTS OF TREATMENT OF FRACTURE OF THE FEMORAL SHAFT*

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THERE were 162 patients with fracture of the femoral shaft admitted to The Roosevelt Hospital from 1910 to 1924. Twenty of these died, 8 from concurrent cranial, thoracic or abdominal lesions, 8 from the fracture or its complications, and 4 later in the course of treatment of the fracture. Counting these latter 4 there were 146 patients treated.

The majority of these patients were children, 86 being in the first decade of life, and 20 between ten and sixteen years of age; and the remaining 40 were adults. One is here considered adult at sixteen, for at this age one has attained a sufficient muscular development to be put in this class so far as the principles of treatment of this fracture are concerned.

The degree of success obtained by treatment is still subject to variable measurements by the profession. Here one-half inch or less of shortening and ninety degrees or more of flexion have been taken as a satisfactory result. This amount of shortening does not cause lameness and can easily be compensated for by a lift in the shoe or an addition to the heel. Also one-half inch is within the range of difference between normal limbs or of the error in measuring them. Ninety degrees of flexion permits one to kneel and to walk without lameness. In other words, the standard is the normal appearance of the patient walking.

The method of treatment most frequently used was that of immobilization by plaster of Paris. Plaster, however, is being more and more reserved for fracture without displacement, so that in later series it will probably be the least frequently used. Forty-six cases were treated by immobiliza-

* Written especially for The Roosevelt Hospital Report, 1924.

tion. The results in 10 cases are not recorded. Eleven were taken out of plaster to be treated by traction, or by operation. Of the remaining 25 cases, 16 had one-half inch or less of shortening (9 having no shortening), 4 had three-quarters inches, 3 had one inch and two had over an inch. Of the 16 with one-half inch or less shortening all had good function; so that 44 per cent met our standard requirements.

For fractures without displacement or those that can be reduced, and reduction maintained, plaster is satisfactory. Of the nine cases with no shortening, 7 were fractures without displacement and the other 2 were reduced and stayed so. But for fractures, the fragments of which do not impinge, plaster is the worst kind of treatment. It should be borne in mind when plaster is used that the traumatic swelling of the leg will subside in time and that with room in the cast the muscles exerting their pull may cause angulation or even displacement of the fragments. A cast may have to be applied anew a couple of times to keep pace with the shrinkage of the leg and correct any tendency to angulation. Eliason* suggests that the leg and thigh be put up in flexion in the cast to prevent as far as possible this tendency by the relaxation of the muscles.

The next most frequent method used was that in young children of suspension of both legs to a frame over the bed. Suspension was attained by adhesive straps placed from as high as the fracture down the sides of the legs and attached to a spreader below the foot. A cord knotted at the end was pulled through a hole in the spreader and run over a pulley hung to the frame. To the loose end of the cord sufficient weight was attached just to raise the child's hips from the mattress. Forty-one children were treated this way. Except for 6 children (2 each at seven, eight and nine years of age) these were under seven. Children older than six need more traction to reduce their fractures than can be obtained by the counter weight of hips only. Four cases were taken down to be operated upon. Thirty-one had one-half inch or less shortening (8 had no shortening); 1 had five-eighths; 2 had three-quarters inches; 1 had one inch; 1 had one and one-half inches, and 1 had no result recorded.

* *Ann. Surg.*, Aug., 1921.

These children all regained perfect function. This method gave 77 per cent success—31 cases out of 40.

Why the 4 cases were taken down from suspension for operation is not stated. The reason probably was failure to reduce by the slipping of the adhesive-plaster traction straps. If the plaster slips it may cause abrasions of the skin or formation of blebs and then traction by this method has to be given up. When the adhesive strap is wide, goes as high as the fracture, is placed on smoothly, reinforced with spirally placed strips, all held by a firm bandage, it should hold the weight required for these cases.

Twenty-eight cases were treated by traction, formerly called "Buck's extension," but nowadays obtained, not in Buck's apparatus, but by suspension of the leg in a Thomas or Hodgen splint from a Balkan frame and traction exerted by a weight pulling over the foot of the bed on adhesive straps applied to the leg. The results in 2 cases are not recorded. Ten cases were failures by this method. Of these, 1 was reduced under ether and reduction maintained by a plaster spica, 2 were treated by skeletal traction and 7 were operated upon. Thirteen had one-half inch or less of shortening and 90 per cent of flexion, 2 had three-quarters inches, and 1, a negro boy with bilateral fractures, (one compound, both later suppurating) had marked shortening and deformity though fair function. This method yielded 50 per cent success—13 out of 26 cases.

Traction applied to a fracture in this manner has a distinct disadvantage. Much of it is expended on soft tissues whose attachments are above the site of fracture and therefore helps not at all toward the reduction. The amount thus expended is estimated as about one-half. Adhesion between plaster and skin will support about 15 lbs. weight. By this method of traction, then, 7½ lbs. is the amount acting on the lower bone fragment to cause reduction. This is sufficient, or nearly so, in those under sixteen years.

At this age the muscular development of the patient has reached a point where more weight as the tractive power is needed, and this can only be obtained by skeletal traction. This method has been used at The Roosevelt Hospital only since 1916. Four cases were treated by nails and 13 by

tongs. Many of the wounds became infected but healed nicely on removal of the nail or tongs. One nail wound, however, was still suppurating when the patient was dis-

FIG. 42. Lateral view fractured femur before treatment.

charged after one hundred and one days in the hospital. Of the 17 cases, 8 had one-half inch or less of shortening (6 had no shortening), but 2 of these had limitation of flexion to forty-five degrees; 3 had three-quarters of an inch, 2 of whom had a double break, 1 of the latter having only 45

FIG. 43. Anteroposterior view nineteen days after traction by tongs.

FIG. 44. Anteroposterior view before treatment.

Fig. 45. Lateral view before treatment.

FIG. 46. Anteroposterior view forty-four days after treatment showing excessive callus simulating clinically myositis ossificans.

FIG. 47. Lateral view. Tongs had been removed twenty-two days after treatment began. No shortening by measurement.

degrees of flexion; 3 had one inch or more of shortening and limitation of flexion, and 1, a woman of sixty-eight years, died of pneumonia well along in her treatment. Two were operated upon, 1 early in our experience of skeletal traction because an angulation could not be controlled, the other because of bedsores. Not counting these last 2 cases this method yielded only 53 per cent of good results.

It does not appear that the method is at fault, but the application of it. It seems susceptible of far greater satisfaction. Traction should not be removed too soon: in fact it should be maintained, however long, until union is firm. One case after three weeks of skeletal traction with complete reduction, regained, under a cast, in a couple of weeks, the original displacement. We have hesitated to use skeletal traction in children for fear of infection extending to the epiphysis. Speed and Eliason, however, recommend it, although the latter reports such an accident.

With all possible effort at conservatism, 37 patients were finally operated upon—every fourth one of the series. Twenty-nine were plated, 1 fixed with a Parliam and Martin band, 1 with kangaroo tendon, 1 with catgut, while 5 had no internal fixation. Though eleven of the plates were removed, the cause for removal was specified only in 6, as follows: delayed union 2; infection 2; refracture through callus and plate, 1, and loose screws, 1. Four of the cases, 11 per cent, were infected, 2 being recognized only at time of removal of the plate. Three patients died of shock, lung abscess, and bedsore septicemia. The latter cannot be classed as an operative mortality. It was felt this patient could be better cared for in a cast than kept flat on his back under a Balkan frame, which position had caused his sores.

Of the 37 patients the results of 6 are not recorded, 24 had one-half inch or less of shortening (19 had no shortening); 1 had three-quarters of an inch; 2 had one inch; 1 had one and one-quarter inches. Two of those with one-half inch or less of shortening, had limitation of flexion to forty-five degrees, causing them to walk lame.

Operation yielded 70 per cent of good results, 22 out of 31 cases, but nearly a 5 per cent mortality, with 2 deaths.

The breaking of a bone causes bruising and tearing of the muscles surrounding it with extravasation of blood into them. In the process of healing, organization and then contraction of the blood and muscles take place. This fixes and stiffens the muscles, and when they pass over a joint, limits the motion of that joint. As operations add considerable trauma to already injured muscles, this probably explains the more frequent limitation of motion after operations.

The tendency toward limitation of motion increases with the age of the patient.

There were 3 cases of delayed union. One of these was treated by skeletal traction and 2 by operation, 1 of these because of non-union, on the supposition that the delay was due to poor apposition of the fragments.

Consideration of the late results in children is most gratifying. Nine children with a total of eight inches of shortening on discharge, when seen three years later, had only two and one-half inches of shortening. Two-thirds of the total shortening had been made up, function was complete and there was no visual and but little palpable evidence of fracture. On the other hand, of two children who had no shortening on discharge, when seen a couple of years later, one had one-half inch of lengthening and the other one-half inch of shortening.

Though we may expect bone growth to be accelerated in the repair of a fracture compensating for any shortening, occasionally producing lengthening, it may sometimes be retarded.

In conclusion it seems that:

The results of the general treatment of fracture of the femoral shaft are not very good.

The use of plaster of Paris is satisfactory only in fracture without displacement or when reduction is possible and immobilization only is necessary to maintain reduction.

Traction by suspension of both legs above the bed for children under six is excellent treatment.

For patients between six and sixteen suspension and traction properly applied and carefully tended should give good results.

Skeletal traction is necessary for adults. With practice in its use results should be nearly perfect.

Operation is unnecessary in children. With the increasing use of tongs operation is less frequently employed on adults. In proper hands, however, it gives nearly the highest percentage of satisfaction.

END RESULTS OF 201 CASES OF CARCINOMA OF THE CERVIX*

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THE following is a report of 201 consecutive cases of carcinoma of the cervix, admitted to the gynecological service of The Roosevelt Hospital, during the period from 1910 to 1920, inclusive—eleven years. During this time there have been a number of changes in the procedure of handling these cases; and since 1917, radium has been used extensively in the great majority of instances, either alone, or preparatory to and following operative removal. For this reason, a study of the end results is not complete without showing their relation to the type of procedure; and the groups shown, in the tables which follow, are so arranged as to bring out this relationship.

No attempt will be made to study these cases with reference to symptoms, signs, or other points of interest in their histories, except to give the age of incidence, state in life, and the relation to child-bearing. Likewise, the pathology will be discussed only as to type and location of growth, with special reference to its bearing on the end results, particularly in those cases which show no recurrence, after three years.

Age of Incidence. The exact age is known in 182 cases, and an analysis by decades shows the following:

Two cases between ten and twenty years, one being twelve and the other nineteen years of age; 7 cases between twenty and thirty; 36 cases between thirty and forty; 76 cases between forty and fifty; 53 cases between fifty and sixty; 5 cases between sixty and seventy and 3 cases over seventy, these being seventy-one, seventy-two and seventy-

* This paper was written especially for The Roosevelt Hospital Report, 1924.

five years of age. Thus it will be seen that 90 per cent of the cases fell between thirty and sixty years, and 70 per cent between forty and sixty years. The average age is forty-five and one-half, the youngest being twelve and the oldest seventy-five years. The age seems to bear little, if any, relationship to recurrence, for the average age of cases free from growth after three years, is forty-one which is practically the average age of incidence.

State in Life, and Relation to Child-bearing. Of the 201 cases, 192, or 95.5 per cent, were married, while 9, or 4.5 per cent, were unmarried. Likewise 181 cases, or 94.3 per cent, bore one or more children, while 11, or 5.7 per cent were primiparae. With such a preponderance of these cases falling among the multiparous women, one naturally forces the conclusion that child-bearing is a definite causative factor in carcinoma of the cervix; but when one considers that the majority of women at forty-five—the average cancer age shown above—are married and have borne one or more children, this conclusion loses some of its importance.

PATHOLOGY

Of the cases included in this report, biopsy with pathological report, from sections, was obtained in 192, while in 9 cases the diagnosis was established only clinically; but in each of these latter the disease was so far advanced as to be practically unmistakable, and was grossly of the squamous variety. Of the specimens examined in the laboratory, 9 or 5 per cent proved to be adenocarcinoma, the remainder, 183 or 95 per cent, being squamous in character. All the cases which have shown no recurrence, after three years, were of the squamous group. As to the age and type of growth, the youngest case, twelve years, showed adenocarcinoma, while the ages of the other cases, in this group, all ranged between forty and fifty years.

A study of the location and extent of growth on admission furnishes several points of interest. These facts have been established, in all but the few classed as inoperable, by pelvic and rectal examination under a general anesthetic, and, in the cases where excision was done, by direct observance at

operation and subsequent study in the laboratory. In only 48 cases the lesion was confined to the cervix alone; in 40, it had extended into the vaginal walls, while in 103 it was decided that the surrounding parametrial tissues were involved. Of the 16 cases alive over three years without recurrence, 11 showed cervical involvement only; 4 showed extension to the vaginal walls, and 1 case beginning extension into the parametrium. Of the cases in which recurrence took place after three years, all but one originally had involvement of cervical tissue only. Thus, in these cases traced, a favorable prognosis depended very materially on whether or not the growth was limited to the cervix.

TYPE OF PROCEDURE

As stated previously, the type of procedure in handling these cases of carcinoma of the cervix has varied considerably, from time to time, during the eleven years covered by the report. Before the use of radium, cases were divided into two groups—the operable and the inoperable—the latter being treated only palliatively, or with such chemicals as acetone. The operable group had either the classical Wertheim type of operation, or a complete hysterectomy, with rather wide excision of the broad ligaments; and both of these were, as a rule, combined with cauterization of the cervix. The latter was accomplished in some cases by the actual, or hot, cautery, and in others by the Percy method. In an intermediate group of cases excision was not attempted, but the cervix alone was subjected to cauterization only, by one of the two methods mentioned above.

After the adoption of the use of radium in 1917, a number of cases were still treated by these procedures, but soon thereafter the present-day methods were developed, and are now treated as follows: Extremely early cases are still considered operable, and receive radiation with the element, both before and after excision. A varying period of from three to six weeks is allowed to elapse between the primary radiation and hysterectomy, and here a modified Wertheim, with exposure of the ureters in their lower course, or a rather wide complete hysterectomy is done. Postoperative radiation in

the healed vaginal vault is begun before the patient leaves the hospital, and is continued later, if the original extent of the growth seems to warrant it. The average preoperative application of radium is 2400 mgm.-hrs. within the cervical canal and growth, while the average postoperative dose is 1000 mgm.-hrs. The element itself is used in silver and brass capsules—one 50- and two 25-mgm. tubes. At present the inoperable cases are treated by repeated radiation of the growth, the primary application usually being 2400 mgm.-hrs., and those following depending upon subsequent examination, and the possibility of vesicovaginal and rectovaginal fistulae.

Table 1 shows the 201 cases grouped according to the type of operative procedure, as well as the number in each group which could be traced with sufficient accuracy as to be considered of value in establishing end-results.

TABLE 1

Operation	Total	Total traced
Hysterectomy		
Wertheim—cautery	41	21
Wertheim—radium	10	9
Total Wertheim type	51	30
Hysterectomy		
Complete—cautery	34	20
Complete—radium	12	7
Total complete type	46	27
Total hysterectomies	97	57
Hot cautery—alone	17	9
Percy cautery—alone	10	8
Radium—alone	50	15
Total operations	174	89
Inoperable (previous to 1917)	27	5
Total cases	201	94

There were 97 hysterectomies, 51 of them Wertheim and 46 complete. Only 30 per cent of the former and 27 per cent of the latter could be traced. Seventeen cases were cauterized with actual or hot cautery only, while on 10 the Percy method alone was used. We have been able to follow 9 of the former and 8 of the latter. Fifty cases received radiation only, of which the outcome is known in 15. The remaining 27 were of the inoperable, advanced group, and were seen previous to the use of radium.

END RESULTS

Of the 201 cases treated, only 94 could be traced and the end results discussed below are based upon this total.

Operative Cases, with No Recurrence, or Free from Growth Three Years or More after Operation. Sixteen cases fall into this group and are shown below in Table II. The only cases

TABLE II

CASES WITH NO RECURRENCE IN RELATION TO OPERATIVE PROCEDURE

Operation	Total traced	3 years	4 years	5 years	6 years	7 years	8 years	9 years	Total
Wertheim—cautery	21	1	1	1	..	..	1	1	5
Wertheim—radium	9	...	..	2	1	..	..	..	3
Total Wertheim	30	1	1	3	1	..	1	1	8
Complete—cautery	20	...	..	1	..	..	1	1	3
Complete—radium	7	1	1	1	..	1	..	..	4
Total complete	27	1	1	2	..	1	1	1	7
Total hysterectomies	57	−2	2	5	1	1	2	2	15
Percy cautery*—alone	8	...	1	..	..	..	..	..	1
Total	65	−2	3	5	1	1	2	2	16
Percentage (excision cases)	57	4.5	4.5	11.4	2.3	2.3	4.5	4.5	34

* This case had ligation of internal iliacs also.

NOTE.—As 13 of these cases died postoperatively, percentages are figured on total of 44.

considered here as possibilities, are those in which some type of hysterectomy was done, except for one case of Percy

cauterization of the cervix and ligation of the internal iliacs, in which there was no evidence of growth four years after operation. This case has not been traced since 1920, and all attempts to locate it have been unsuccessful.

It will be seen that 2 cases have gone between three and four years without recurrence; 3 cases between four and five years; 5 cases between five and six years; 1 case between six and seven years; 1 between seven and eight years; 2 between eight and nine years, and 2 between nine and ten years. Eleven, or more than two-thirds, of these cases are over five years. Thus, of the 57 cases traced, which had some type of hysterectomy, 15 are known to be alive without recurrence more than three years, or a total of 34 per cent for successful results in the operative cases. A correction of percentage is necessarily made, as 13 of this group died postoperatively in the hospital.

The table also shows the type of operative procedure, and here the results indicate practically as much success where complete hysterectomy was chosen, as where the more extensive Wertheim was done. If any operative group can be said to have shown more success than the others, it is where one of the two types of hysterectomy was combined with radiation. This fact would seem to justify the present method of treatment described above for operative cases—that is, wide complete hysterectomy, with preoperative and postoperative radiation.

Operative Cases with Known Recurrence. Here again only cases in which some form of hysterectomy was done are considered, and they are summarized in Table III.

All these showed recurrence within the pelvis, the majority in the remaining parametrial tissues; a few locally in the vaginal walls, and only one to some distant organ, in this case the parotid gland. Nine cases had recurrence in six months, 7 more in twelve months, 2 more in eighteen months, 3 between eighteen months and two years; 4 more in three years; 2 more in four years, and 2 more in five years. Thus, of the 57 operative cases traced, 29 or 66 per cent are known to have had recurrence, and of these 55 per cent recurred within one year, 86 per cent within three years, 14 per cent between

three and five years. No cases going over five years have shown recurrence to date.

This table also shows the type of operation in relation to time of recurrence; but little if any conclusion can be drawn from this comparison. Sixteen cases had had Wertheim and 13 complete hysterectomy. Up to three years, 15 of the

TABLE III

SHOWING TIME OF RECURRENCE IN RELATION TO OPERATIVE PROCEDURE

Operation	Total traced	6 months	1 year	18 months	2 years	3 years	4 years	5 years	Total
Wertheim—cautery	21	3	2	..	1	3	1	..	10
Wertheim—radium	9	2	2	..	2	..	..	..	6
Total Wertheim	30	5	4	..	3	3	1	0	16
Complete—cautery	20	3	3	1	..	..	1	2	10
Complete—radium	7	1	..	1	..	1	..	..	3
Total complete	27	4	3	2	0	1	1	2	13
Total hysterectomies	57	9	7	2	3	4	2	2	29
Percentages of total	44	20.5	15.9	4.5	6.8	9.1	4.5	4.5	65.9
Percentages of recurrences	..	31.0	24.0	7.0	10.0	14.0	7.0	7.0	

NOTE.—Recurred in three years, 25 (85 per cent); over three years 4 (14 per cent). Percentages are figured on a total of 44.

former and 10 of the latter had shown recurrence, while after three years 1 Wertheim and 3 complete hysterectomies developed further lesions. Comparison of these figures with the total cases traced for each operative group, shows approximately a 50 per cent recurrence in each.

Deaths. Table IV gives a statistical study of all deaths, showing the relation between the time of death and the type of treatment, whether excision, cautery or radium alone.

Of the 57 cases which had hysterectomy, 13 died postoperatively in the hospital and are analyzed as a special group below; 6 died within 6 months, 6 more within a year, 5 more in two years, 8 more in four years, and 3 more in six years.

TABLE IV

SHOWING TIME OF DEATH IN RELATION TO OPERATIVE PROCEDURE

Operation	Total traced	P.O.	6 months	1 year	18 months	2 years	3 years	4 years	6 years	Total
Wertheim—cautery	21	6	3	2	..	..	2	2	1	10
Wertheim—radium	9	..	1	2	1	...	1	...	1	6
Total Wertheim	30	6	4	4	1	0	3	2	2	16
Complete—cautery	20	7	2	1	2	1	...	2	1	9
Complete—radium	7	....	....	1	...	1	1	.....	.....	3
Total complete	27	7	2	2	2	2	1	2	1	12
Total hysterectomies	57	13	6	6	3	2	4	4	3	28
Percentages	44	13.3	13.6	13.6	6.8	4.5	9.09	6.8	6.8	63.6
Hot cautery—alone	9	....	4	1	1	2	...	1	...	9
Percy cautery—alone	8	....	4	2	...	1	...	...	...	7
Total cautery	17	....	8	3	1	3	0	1	0	16
Radium—alone	15	....	6	2	2	2	2	0	0	14
Total	89	13	20	11	6	7	6	5	3	58
Percentages	76	7.5	26.3	14.5	7.9	9.2	7.9	6.6	3.9	76.3

NOTE.—Of the 27 inoperable cases treated palliatively, only 5 could be traced, and all died within six months.

The last 3 had shown recurrence in two, three and five years, respectively, but life was prolonged until the sixth year in each case by radiation. Thus of the 57 cases mentioned above, 44 left the hospital, and of these 28, or 63 per cent, died of cancer within six years, 21 or 75 per cent of the deaths occurring within three years. One additional case, free from growth four years after operation, died of pneumonia. One other case, developing recurrence five years after excision, is still living two years after the recurrence was noted, but in very

poor health. Of the cases leaving the hospital, approximately just as many died of cancer following Wertheim as following complete hysterectomy.

Seventeen cases were traced which had been treated with hot and Percy cautery. Of these all but one were dead within three years, and 70 per cent of these deaths occurred within one year.

Only 15 cases treated by radium alone could be traced, and of these 14 were dead within three years, 60 per cent of these deaths occurring within the first year. The remaining case is still alive, three years after first radiation, but the growth is well advanced and the patient has a rectovaginal fistula.

Of the 27 advanced inoperable cases that received nothing but palliative treatment, only 5 could be traced, and all these died within six months.

Thus a summarization shows a grand total of 76 (or 80 per cent) of deaths due to cancer, out of the 94 cases traced.

Postoperative Deaths. An analysis of the 13 cases dying in the hospital, after operation, follows:

From 1911 to 1920, there were 97 hysterectomies, 51 of Wertheim and 46 of the complete type. Thirteen of these cases, or 13.3 per cent, died postoperatively in the hospital. All these deaths occurred between 1911 and 1915, during which period 64 of the hysterectomies were done. From 1916 to the end of 1920, 33 cases had hysterectomy (17 Wertheim and 16 complete) but in none of these did death result from operation. Of the 17 cases treated by hot cautery and the 10 by Percy cautery, none have died in the hospital. Likewise, there have been no fatal results from treatment by radium, either alone or combined with hysterectomy, there having been 50 of the former and 20 of the latter, in the period covered by the report. Thus, of the 174 cases having some type of operative procedure, in 13 only (or 7.5 per cent) can it be said that death resulted from operation.

In these postoperative deaths, the average age of the patient was forty-eight. One case died on the table, and 6 others died within seventy-two hours; 2 died from pneumonia (one on the fourth and the other on the fourteenth

day); 1 death on the eighth day was due to ileus; and in 3 other cases (one on the eighth, one on the eleventh and one on the eighteenth day) death resulted from circulatory complication. Six had had Wertheim and 7 the complete type of operation. In 4 the growth was confined to the cervix; in 3 the vaginal walls were also involved, while in 6 there was beginning extension to the parametrium.

TABLE V

SHOWING RELATION OF DEATH TO RECURRENCE

Recurrence in	Total	Died after recurrence in					
		6 months	1 year	18 months	2 years	3 years	4 years
6 months	9	6	1	2			
1 year	7	5	1	..	..	1	
18 months	2	1	1				
2 years	3	..	2	..	..	..	1
3 years	4	2	1	..	..	1	
4 years	2	2					
5 years	2	..	1	..	(1 live)		
Total	29	16	7	2	1	2	1

Relation of Death to Recurrence. In Table v, the relation of time of death to recurrence is shown. Of the 29 cases showing recurrence at various periods from six months to five years, 16, or 55 per cent, were dead six months later, while 7, or 24 per cent, lived only one year, making a total of 23, or 79 per cent, who died within twelve months. Thus the length of time between operation and recurrence has no relation to, or effect upon, the time of death after recurrence; as the cases where carcinoma reappeared three, four and five years after operation, died just as soon as those in which the postoperative free interval was of much shorter duration. Two patients died three years, and one four years, after recurrence, while 1 is still alive, four years after the growth reappeared. All 4 of these cases have been exten-

sively radiated, and this accounts in some measure for the prolongation of life.

Radium Cases. Since 1917, 72 cases have been treated by radiation, either alone or combined with some type of excision. Fifty cases, having been considered inoperable, have had radium only, while 22 were radiated in conjunction with hysterectomy. Wertheim was done in 12, and complete hysterectomy in 12, of these 22 cases. Eight of them received radiation before, 4 after, and 10 before and after operation. The average amount before was 2000 mgm.-hrs. and the average postoperative application was 1000 mgm.-hrs. In the group of 50 cases treated by radium alone, the smallest total amount used was 1200 mgm.-hrs. (this case failing to return for further treatment), while the largest amount was 7200 mgm.-hrs., in four applications. The average total application was 4000 mgm.-hrs.

Of the 22 operative-radium cases, only 16 could be traced. Of these, 7, or 44 per cent, have remained without recurrence—1, three years, 1, four years, 3, five years, 1, six years and 1, seven years. The remaining 9, or 56 per cent, have all developed recurrence—3 in six months, 2 in one year, 1 in eighteen months, 2 in two years and 1 in three years. Of these 9, all are dead—6 dying within six months, 2 within twelve months, and 1, four years after the recurrence.

The latter case is of particular interest. Six years ago she had a Wertheim hysterectomy, with 2400 mgm.-hrs. radiation before, and 600 mgm.-hrs. after operation. Two years later, recurrence developed as a small nodule in the anterior vaginal wall near the urethra. In the past four years since its reappearance, the growth has been radiated three times for an additional 2150 mgm.-hrs., the last application having been about one year ago. Within the past six months an indurated, ulcerated area developed on the anterior vaginal wall, and metastatic masses have been noted within the pelvis. The patient's death has been reported within the past few weeks. Undoubtedly radiation very materially prolonged life in this case.

Of the 50 cases of advanced carcinoma of the cervix treated with radium alone, unfortunately only 15 have been traced. This is due to the fact that the majority of them were treated

during the recent war period (from 1917 to 1919), when the follow-up system was greatly handicapped by a limited personnel, and by frequent changes in the patient's address.

Fourteen, or 90 per cent, of those traced have died of cancer, 6 within six months; 2 more within a year; 2 more in eighteen months; 2 more within two years, and 2 others lived three years. The remaining 1, while still alive three years after the first radiation, is in fair health, but has a rectovaginal fistula, and the growth is well out into the parametrial tissues. This case has had 5,200 mgm.-hrs. radiation, in four applications. Two others had fistulae, one rectovaginal and one vesicovaginal.

Thus 60 per cent of these advanced cases died within twelve months, and of the others, only 1 had lived more than

SUMMARIES

Total number of cases	201	
Inoperable—palliative	27	
Total operative cases	174	
Total hysterectomies (Wertheim 51)	97	
Total cautery cases	27	
Total radium cases	50	
Total cases traced (inoperable—5)	94	
No recurrence or free from growth	16	34 per cent
Recurrence, but not dead	1	2 per cent
Died, postoperative	13	7 per cent
Recurrence, and dead	28	63 per cent
Recurrence in less than three years	25	57 per cent
Recurrence after three years	4	9 per cent
Alive three years, without hysterectomy (radium cases—1; cautery, 1)	2	6 per cent
Dead, without hysterectomy	30	94 per cent
Total dead in less than three years	68	72 per cent
Total dead after three years	8	9 per cent

three years. All showed marked regression of the growth locally within the cervix and vaginal walls, the majority shrinking down so that their offensive discharge and bleeding were completely controlled. In many the lower parametrial involvement also showed some recession, and their general health was materially benefited for a time. Further spread of the growth outward, usually marked by deep pelvic and sciatic pains, could only temporarily be controlled, for at

this stage additional radiation was usually limited by the danger of vesicovaginal and rectovaginal fistula. At present these cases are also receiving cross-fire *x*-radiation of the pelvis, in addition to radiation within the cervix. Future reports will undoubtedly show even better control of the parametrial involvement.

In the past three years, 1921 to 1923, an additional group of 46 cases of carcinoma of the cervix have been treated. Thirty-one were of the advanced type and had radium alone, while fifteen were considered sufficiently early to have hysterectomy after radiation. These end results are not included in this report, as the usual three-year period has not elapsed, but the percentage of those free from growth to date is most promising, and should be even higher than the figures given above for the preceding ten years.

CONCLUSIONS

1. *Advanced Cases.* This group, when treated by radium alone shows much better results than were formerly obtained by any other nonoperative palliative procedure, or by such operative measures as the use of the actual or Percy cautery. The growth locally in the cervix and vaginal walls can be controlled, so that the patient is infinitely more comfortable than formerly: and the parametrial involvement can for a long period be held in abeyance, especially if radiation is combined with external *x*-radiation. Treatment with radium in such cases is a safe procedure: for in none of the 81 cases radiated in the past seven years, has death resulted from its use.

2. *Early Cases.* This group, when subjected to hysterectomy, shows 34 per cent free from growth three years or more after operation; 25 per cent free five years or more; and where hysterectomy was accompanied by radiation, 44 per cent had no recurrence three years or more, and 31 per cent five years or more after the removal. These results compare very favorably with the figures reported by those clinics where radium is available in large amounts, and radiation alone is the adopted method of treatment. Thus, where radium can be used in limited amounts only (such as 100

mgm. of the element) and the method of application must necessarily be limited also, hysterectomy plus radiation is still the method of choice in early cases. Here too the safety of such procedure, from the standpoint of postoperative mortality must be emphasized. None of the 37 cases of hysterectomy combined with radiation, has died as a result of operation.

As *x*-radiation will also be included hereafter in the operative procedure of this group, future end results should show an even higher percentage of five-year cures.

CLINICAL RECORDS WITH AUTOPSY REPORTS OF PULMONARY CASES

DAVENPORT WEST, M.D.

THE object of this paper is to present a series of pulmonary cases accompanied by clinical records with autopsy findings.

It is through the courtesy of Dr. Rolfe Floyd that the pathologist's reports are incorporated. His assistance in the preparation of this article is gratefully acknowledged.

CASE I. Lobar pneumonia with unusual modifications of the lesion:
Infarcts
Coagulation necrosis
Connective tissue in the exudate
Thrombosis of pulmonary artery

The patient was a white woman thirty-five years of age, who had been well until the present illness, except for having had occasional coughing attacks and the occasional occurrence of blood in the sputum.

The present illness was of two days' duration. The onset was with chill, fever and cough, followed by what she characterized as a heavy cold.

Physical Examination. The noteworthy findings were confined to the chest. There were signs of consolidation involving the upper and middle lobes of the right lung, and the upper lobe of the left lung.

Blood Count. White blood cells 38,000 per cm. with 97 per cent polynuclear neutrophiles. The sputum contained Group II pneumococcus; blood culture remained sterile. Wassermann reaction was negative. The course was that of a severe pneumonia, failure of resolution and death on the twenty-fifth day.

Autopsy Findings. Right Lung. Upper and lower lobes extensively consolidated. In the lower part of the lower lobe is a dense, rounded, whitish area 2 cm. in diameter, which exudes a little pus at the center and does not show the fibrosis, calcification or other features of a tubercular focus. Microscopically this proved to be an area of coagulation necrosis. In the upper and outer aspect, about under the shoulder joint, is an irregular lobulated and oblong cavity 6 cm. in maximum measurement, containing thin brown pus; and also a large necrotic mass, somewhat adherent to the wall and looking like a sequestrum in a bone abscess. There is no offensive odor to the abscess. The wall is formed by a thin, whitish and quite distinct membrane. The right middle lobe shows a little patchy congestion at its upper posterior angle. Apart from consolidation the lungs show edema without noticeable congestion.

Left Lung. The left lower lobe is completely and unevenly consolidated. Behind at the base is a very large, dark red infarct, wedge shaped, 7 cm. from the costophrenic border to the apex of the infarct, into which a thrombosed vessel runs. In the axillary region there is a very large abscess cavity roughly 8 by 11 cm. containing 8 oz. of thin, brown pus. Its walls are brownish-black and necrotic, but marked off from the living lung by a yellowish-white membrane, thinner than the one around the abscess in the right upper lobe. There is no offensive odor. The outer wall of the abscess is so thin that it ruptures even on very careful removal of the lung. At the apex of the lobe is a small lobulated, yellowish-white area, 2 cm. in maximum diameter and of a firm and even consistency throughout. It shows no calcification or fibrosis, is sharply marked off from the surrounding tissue, and proved, under the microscope, to be an early abscess. The upper lobe shows the same irregular consolidation as the lower, and there is also a small, whitish-yellowish area, such as that just described.

The left pulmonary artery contains a large thrombus which practically occludes the lumen of the branch leading to the large abscess.

Comment. The consolidated areas showed microscopically in several places typical organization of the intra-alveolar exudate. It is unusual to find in a single specimen a pathological picture with such a variety of interesting features.

Case II. Cyst of the lung.

A white woman, sixty-seven years of age, was admitted to the service of Dr. Kirby Dwight. Her complaint was a painful swelling in the abdomen. There was nausea and some vomiting; no bowel movements for forty-eight hours, although she had taken cathartics. There were the physical signs of an irreducible hernia in an old operation scar. The abdomen was opened and a band from the ascending colon to the transverse was found causing a kink in the hepatic angle. This band was divided with relief.

After the operation, there was persistent fever. Blood examination: white blood cells 9,600, polynuclears 90 per cent; later, white cells 20,400, polynuclear 85 per cent. No blood was found in the feces. No tubercle bacilli were found in the sputum.

Roentgenographic Examination showed a dense shadow on the left side extending from the apex to the second rib, and a hazy shadow extending from the sixth to the eighth rib; diagnosis, pulmonary tuberculosis.

Three weeks after operation there were signs of a pneumonia. The patient gradually became more and more ill and died fifty-four days after the operation.

The anatomical diagnosis included the following:

Left Lung, large apical cyst. Acute endocarditis with vegetation, tricuspid; purulent meningitis; patchy pneumonia, right lower lobe; complete pleural adhesion, left; peritoneal adhesions about the gall-bladder and ascending colon; enormous gall-stones of common duct; distended gall-bladder; atrophy of pancreas with cystic distention of ducts; chronic nephritis; aortitis with dilated arch.

A description of the lung cysts: The left pleural cavity is obliterated by adhesions which are especially dense at the apex. The left lung contains but little air after removal, but is otherwise normal, except for a large cyst, 8 by

4 by 4 cm. which occupies its apex. The wall of the cyst is of dense, white fibrous tissue and is smooth inside with a few shallow accessory depressions on its lower wall. There is no inflammatory reaction about it. Its contains a brownish, amorphous matter resembling pasty feces, but without odor.

Microscopic Examination. Lung 1. The cyst wall is lined with epithelium closely simulating that seen in the large bronchi; the outer margin shows no cilia, but often a dark straight margin; there are goblet cells in places. There are mucous glands in the submucosa. Behind this mucous layer is a dense laminated fibrous wall with thick vessels and foci and streaks of round cells. One part of the section shows some lung tissue which is the seat of advanced interstitial pneumonia with great thickening of alveolar walls, embryonal alveoli, much pigment and many much dilated bronchi.

Lung 2. Similar to 1, but the wall is lined with a granulation tissue, except for one epithelial area. The epithelium shows definite cilia. The interstitial pneumonia of the neighboring lung is excellently shown, especially a group of embryonal alveoli and some small alveolar crypts.

Comment. In this case, the autopsy findings definitely established the fact that the roentgenographic shadows were caused by a lung cyst and not by tuberculosis.

Case III. Fibrinous bronchitis.

A woman thirty-four years old was admitted to the hospital with the history of an acute illness of three days' duration. The onset was sudden, with cough, chill and fever, vomiting, headaches, pain in the chest and prostration. She gave a history of pneumonia three times, the last attack nine years ago. Seven years ago she had "pleurisy" and shortly thereafter was admitted to a tuberculosis hospital where tubercle bacilli were found in the sputum. Several months later tuberculous peritonitis developed. Tuberculous lymph glands of the mesentery, mesocolon and appendix were removed with resulting improvement in the patient's general condition. Then she was up and about, feeling fairly well until the present illness.

At the time of admission her breathing was not particularly rapid, but was frequently interrupted by cough. She looked sick, though not in pain. No definite signs of pneumonia were found. Two days later there was evidence of an area of consolidation in the upper part of the right lower lobe.

Blood Count. White cells 6,100 per cm., polynuclears 64 per cent, lymphocytes 36 per cent. Later; white cells 11,000 per cm., polynuclears 81 per cent. No tubercle bacilli were found in the sputum. The general condition rapidly became more grave. The temperature ranged from 103 to 105°. Death followed on the fifteenth day.

The autopsy revealed double lobar pneumonia, bronchitis with fibrinous exudate, old tuberculosis (healed) of right lung and peritoneum, bronchial and mediastinal glands. The bronchi in the substance of the right lung were deeply congested and contained fibrinous casts together with serum and mucopus. Microscopic section showed the bronchial wall congested, very edematous and extensively infiltrated with round and endothelial cells. The mucosa was damaged but showed individual cells well. The fibrinous plug did not fill the lumen.

Comment. It is of especial interest to report a case of verified fibrinous bronchitis.

Case iv. Lobar pneumonia and lymphatic leucemia.

This case is reported because of the fact that the autopsy shows the lung picture of coexisting pneumonia and leucemia.

The patient was a woman thirty-three years old with the history of an illness of seven days' duration, with severe cough, prostration, and pain in the right chest. She was very ill and was much cyanosed. Respirations were painful. There were signs of a right lower-lobe pneumonia.

The axillary and inguinal glands were enlarged and firm. The liver and spleen were not palpable.

Blood Examination. Hemoglobin 74 per cent, red cells 2,092,000 per cm., white cells 164,000; all the cells were mononuclears. Death followed the day after admission to the hospital.

Microscopic section showed lymphatic leucemia, edema and consolidation of the upper part of the right lower lobe.

The tissue contained much air, but there was a good deal of serum and some epithelium and pus cells scattered through the spaces. In one corner of the section there was a group of alveoli filled with an exudate of partially necrotic cells; epithelium and pus cells predominated and round cells were present, but not a feature. The vessels, large and small, contained an enormous number of lymphocytes, but there were no hemorrhages. The walls of a large bronchus showed no extra-vascular round-cell exudate or foci, nor did such occur anywhere in the section, except one minute one in the wall of a smaller bronchus.

The weight of the spleen was 600 grams. The splenic pulp was packed with lymphocytes and was congested.

Case v. Necrotic bronchopneumonia.

The patient was an infant one month old, who had always been undernourished. For twenty-four hours before coming to the hospital she had been coughing, she was cyanotic when moved and was dull mentally. She had had three convulsions lasting one-half a minute each, in which she screamed, frothed at the mouth and became rigid.

The most striking feature was attacks of extreme cyanosis. Breathing was very rapid and shallow. Death occurred the day after admission.

Autopsy Findings. The left lung shows a deep reddish-purple patch on the lower posterior surface of the upper lobe where this lies against the lower within the interlobar incisure. There is a little fibrin on the pleura over it, but otherwise the left pleura is normal. On section it is an area about 3 cm. in maximum diameter extending from the hilus out to the periphery, but not wedge shaped. It is evidently solidified and there are some pin-head yellow spots in it which exude drops of pus when squeezed. There are no peribronchitic zones on its margins, which fade quite rapidly, but not suddenly, into the surrounding normal tissue. The rest of the lung is pink and completely aerated, and shows no gross bronchopneumonia and no pus in the small bronchi. The microscope showed deep necrosis of the bronchial walls. This lesion belongs to an unusually malignant type of bronchopneumonia.

Case vi. Lobar pneumonia (Friedlander bacillus).

This case showed Friedlander bacillus in cultures from the lung taken post mortem. The cut section revealed lobar pneumonia with abscess formation and with interstitial pneumonia.

The history was that of a woman, twenty-seven years old, who, five days prior to admission, had an attack of vomiting, followed by fever, pains in the right lower chest and cough with blood-streaked sputum. There was no chill. She gave a history of having been treated for pulmonary tuberculosis for one year.

Examination. There was marked prostration, and lips were cyanosed. There was some edema of the feet. Respirations were rapid with limited excursion on the right side.

In the urine there was a trace of albumin and many granular casts with a specific gravity of 1.010.

Blood Examination. White cells 8,000, polynuclears 88 per cent, red cells 4,300,000, hemoglobin 75 per cent. Pneumococcus, Group IV, was recovered from the sputum. The blood pressure was 112/50.

The temperature ranged from 100.8° at time of admission to 101.8°, and two days later became subnormal. Death occurred on the eighth day.

Autopsy Report. The upper lobe of the right lung is densely consolidated, many areas being ordinary mottled hepatization, but numerous lobules in the central and upper portions being of a whitish, granular appearance exuding pus and presenting all the gross features of early abscess formation. The cut surface of this lobe exudes a very tenacious dull red grumous fluid which suggests a mucosus organism.

Microscopic Section. Much of the exudate is predominately pus and fibrin. In many of the alveoli the fibrin reticulum looks finer and much more blurred than usual, suggesting an admixture of a mucoid element. On the margin of the section there is a group of alveoli containing a large proportion of blue-staining, mucoid substance. The pleura is congested and coated with fibrin and pus. There are some hemorrhages along the alveolar walls.

Another section shows the acute process with some zones of early abscess formation where the space walls are less prominent, their vessels empty of blood and collapsed and their nuclei pycnotic. In a few alveoli there are dense plugs of recent fibrin, some elongated nuclei in them, the early stage of intra-alveolar organization. Near one end of the section there is a considerable area of typical organized intra-alveolar pneumonia of longer standing. The plugs are still dense and red, but contain many fibroblasts and some new blood vessels. The alveolar walls are markedly fibrosed and thick. The appearance is absolutely typical of organization of an intra-alveolar exudate of at least one month's duration, and very probably much longer.

This is doubtless the process which was called tuberculosis and for which the patient had been treated for one year. There is not the least evidence anywhere of a tubercular lesion, so she presumably had a lobar pneumonia of the right upper lobe followed by organization about one year ago. The importance of the differentiation is obvious.

Case VII. Sacculated empyema with calcified walls.

A man, seventy years old, while crossing the street was struck by a cab-horse's hoof. He was brought to the hospital and died shortly thereafter.

There were multiple fractures of the ribs of the left side and edema and congestion of the lungs.

The following unusual condition existed:

The left pleura is obliterated by extensive, old and quite dense adhesions. Lying on the inner surface of the left ribs about in the mid-axillary line and densely adherent both to ribs and lung is a flattened bony structure about 6 cm. wide, 21 cm. long and 1½ cm. thick. Its long axis is vertical; its lower end does not reach the site of recent injury. On cross section it contains a cavity filled with a soft, white, cheesy substance, surrounded by extensively calcified walls, the surface near the lung being more calcified than that applied to the ribs. It appears to be the remains of an old sacculated empyema.

Comment. The existence of this queer, flattened, bony structure within the pleural cavity was entirely unsuspected. Its presence was discovered only by autopsy.

Case viii. Fibropurulent mediastinitis.

This patient was a white woman, twenty years old, whose general health had been only fair. She had had attacks of asthma since childhood, but felt fairly well until ten days before admission to the hospital. Then she began to notice soreness of the throat. Five days later she had pain in the left side of the chest and abdomen associated with cough, chills, fever and vomiting.

Physical Examination. A well-nourished young woman, much prostrated and very ill. The tonsils were slightly swollen and red. The neck was swollen and tender about and below the thyroid. Heart action was rapid and regular. There was slight dullness at the base with occasional sibilant sounds.

The urine showed many hyaline and granular casts.

Blood Examination. Red cells 4,102,000 per cm., white cells 38,400, polynuclears 87 per cent.

Roentgenogram showed a thin layer of exudate in the left chest. Temperature ranged from 103° to 106°, pulse 120 to 144, respirations 32 to 40. Death occurred three days after admission to the hospital.

Autopsy Report. On opening the chest the anterior mediastinum is filled from diaphragm to neck with a massive exudate of pus and fibrin. The pericardium is normal. Both pleural cavities contain about 500 c.c. each of a thin pus, and the parietal and visceral layers are extensively coated with a very thin exudate of fibrin. The lungs are congested and slightly edematous, but there is no consolidation anywhere.

Comment. The fibropurulent mediastinitis was the outstanding feature of this case. There was no other known etiology than that described above.

Case ix. Malignant chorio-adenoma with lung metastases.

The patient was a woman forty-one years of age, who had had scarlet fever as a child. She had not had rheumatism. She had had four children: all hard labors. The youngest child was four months old. During the last pregnancy she had much nausea and edema of the feet. There was an instrumental delivery followed by hemorrhage, but there was a satisfactory convalescence, except for some digestive disturbances and occasional cough. For three weeks before coming to the hospital she had been spitting up blood. Nocturia, dyspnea and dropsy came on and rapidly increased during the last week. There had been epigastric pain and vomiting for three days.

Physical Examination. The patient was pale and sallow, slightly cyanotic, with extreme dyspnea and orthopnea. The heart was enlarged and the sounds

were of poor quality. There were some fine râles at both bases, but no signs of pulmonary consolidation.

The urine showed a specific gravity of 1.018, trace of albumin, red blood cells and many granular and cellular casts.

Diagnosis. Cardiac decompensation, pulmonary edema, probable mitral stenosis.

Autopsy revealed chorio-adenoma of the uterus with metastasis in vagina, bladder and lungs, and fatty degeneration of the heart muscle, fatty liver, and degeneration and slight chronic inflammation of the kidneys.

The report is as follows: On opening the abdomen the uterus rises a hand's breadth above the pubis; the fundus presents three rounded confluent eminences, dark-purplish in color and softer than fibroids. On section the tumors in the uterine wall look as if composed of clotted blood among fibrous trabeculae, not unlike placental tissue. They form three masses which run insensibly into each other and at their margins merge into the uterine wall. They measure about 7 cm. in diameter.

Both lungs are densely sprinkled with small hard nodules averaging ½ cm., often confluent to form zones 2 cm. in maximum diameter. These zones are sometimes brick-red, sometimes hemorrhagic on section. They are never white nor umbilicated. They are evenly distributed through all the lobes, equally numerous at the surface and in the central portions; a few have a central spot of hemorrhage, and some show a lighter colored peripheral zone. They look very like zones of bronchopneumonia, except for a few on the interlobar pleural surface which stand up from the surface as never seen in pneumonia. The lung between the nodules is edematous but often not much congested, so that on the surface the sharp color contrast gives a calico appearance. The hilus and tracheal nodes show nothing but anthracosis.

A section of one of the large zones of consolidation proves it to be made up of several small, more or less hemorrhagic infarcts. The lung tissue is dead, the alveolar structure mostly distinct and the spaces filled with blood and fibrin. In a small central area there occur rounded zones of necrotic fibrin with no trace of alveolar architecture, apparently a zone of hemorrhage with secondary necrotic changes. The pleura bounds the consolidation externally, but is not necrotic. In its deeper layers are scattered a few large, deeply staining nuclei which look like strangers and resemble the nuclei seen in the uterine tumor. The surrounding lung tissue shows an exudate of serum, a little fine fibrin, red cells and much epithelium, but no pus cells. The small bronchi are not inflamed.

This case is particularly interesting because the true nature of the patient's condition, the malignant chorio-adenoma and the metastases were satisfactorily explained by autopsy.

Case x. Gangrene of the lung.

The patient was a man thirty-five years old, who gave a history of an illness of indefinite duration accompanied by fever and cough, with prune-juice sputum. The lungs showed some dullness below the angle of the right scapula without other signs, save for a few râles at both bases.

Blood Examination. Hemoglobin 50 per cent, red cells 2,500,000 per cm., white cells 2,200 (repeated and confirmed). Polynuclear neutrophiles 2 per cent,

transitionals 5 per cent, large lymphocytes 65 per cent, small lymphocytes 32 per cent. The slide showed secondary anemia.

Urine was normal except for a trace of albumin. Wassermann reaction was 4 plus. Sputum was negative for tubercle bacilli.

Temperature ranged from 99.2° to 105.4°. Death occurred six days after admission to the hospital.

Autopsy Report. The right lung shows congestion and edema, but in addition, a number of scattered hemorrhagic zones of consolidation which may be either secondary pneumonia or a true bronchopneumonia. In the upper part of the lower lobe, just back of the root and in the mediastinal aspect of the lung is a cavity about 7 cm. in maximum diameter, with ragged necrotic walls, and blackish, grumous contents. No definite gangrenous odor was made out.

This concludes the report of 10 cases with unusual pulmonary findings. These cases illustrate difficulties of pulmonary diagnosis, and show how easy it is to be in error when the clinical features seem simple.

BREAST TUMORS[1]

WILLIAM CRAWFORD WHITE, M.D.

I HAVE selected this subject because it is a topic that should interest all medical men. Certain advances may be made in the treatment of these tumors, but only when the physician and the surgeon make a working team. And it is now especially important because of the new aspect thrown upon the problem by the use of deep *x*-ray therapy and radium. I have the hope that this paper will encourage some of the "*x*-ray alumni" to give us the result of their work with these tumors.

This paper is based entirely on the cases that we have treated at The Roosevelt Hospital plus a rather superficial survey of the work of other clinics. In many respects it is of advantage to have a paper written from one clinic rather than to have it based upon the review of reports from other clinics, some of them unknown personally.

At Roosevelt, since 1915, it has been my good fortune to see most of the pathological specimens that have been removed; and with this opportunity there has been gained a working knowledge. We have tried to be open to conviction; and if not always as open as we might have been, we have had conviction forced down our throats by the unmerciful histological specimen or the follow-up note. My colleagues have been most kind and helpful, and have been more than decent in overlooking some of my errors of pathological judgment. At times, I think, they have imagined that I was not reciprocating. Since I have been on the operating staff as well, they perhaps have noticed that I have developed a view that was more balanced—at any rate, more respectful.

Dr. Finney says that "a tumor in the breast is better out than in." We have followed that policy at the hospital, and we cannot lay too much stress upon it.

[1] Read before The Roosevelt Hospital Alumni Association in November, 1923.

The teaching of a few years ago had the result that the average student thought of cancer of the breast as a disease characterized by retraction of the nipple, orange-peel effect to the skin, and a mass that was fixed to the superficial and to the deeper structures, together with palpable axillary lymph-nodes. Of course such is usually a cancer. But we are not going to make much advance if we wait for that stage of the growth. We must recognize the cancer early and treat it. What we want to watch for is any nodule in the breast, and even in the caked breast of pregnancy to be aware of the possibility of malignancy; also to make a breast palpation part of a routine examination.

The more we see of breast tumors before and after operation the more hesitant we are about making a definite statement that this or that tumor is benign. Case after case has come under our observation which has been watched by a medical man for months before operation was advised. On the other hand, more often we have seen the patient who was advised to come for treatment, but has put it off. In both of these cases we have found cancer with metastases at operation. In early cases one cannot make a definite diagnosis. The best that one may do is to make a definite guess and assure the patient that a local excision will be made, followed by a frozen section, and then get permission to do what is best indicated.

BENIGN TUMORS

Benign tumors comprise about 41 per cent of the cases admitted to the hospital. We have the *single cyst* which is definitely benign, the *localized cystic mastitis*, and the *generalized cystic mastitis*, almost always benign—only once have I seen it associated with cancer. Then we have the *papillary cyst* which is said to be precancerous (whatever that may be). We have had no bad results in excision of these tumors. Then in the solid tumors we have the various types of adenofibroma, in which, at operation, much stress is laid upon the presence or absence of a capsule and the frozen microscopical section. By capsule we do not feel that it is always sufficient to see a fibrous tissue surrounding the tumor. One must make sure that this fibrous tissue covers

all the surface. For it has been our fortune to see the capsule well marked in one area and absent in another part. We are most happy and most certain when the solid tumor can be shelled out.

Tuberculosis and chronic pyogenic mastitis may be mentioned in passing as tumors that are often not recognized until after excision.

We feel that the local excision is sufficient in all these except the general cystic mastitis, the tuberculosis, and the chronic pyogenic mastitis; and in these simple mastectomy is sufficient.

In operative technique we advocate the curved incision at the lower border of the breast with a V-shaped excision from the posterior surface of the breast. This leaves a good cosmetic result and allows the breast to fall down over the scar. When at times it seems necessary to remove all the breast tissue, this may be done through the same incision so as to leave the nipple and skin. And then a puckering stitch behind the nipple may help to keep it from flattening out. A drain may or may not be left in.

For a while the result does not appear altogether wonderful, but in time the breast takes on a contour that compares well with the other breast. And this is much more satisfactory to the patient than an amputation.

Incidentally it may be well to state here that all the tissues are given a careful examination again in the laboratory, and that permanent sections are made and studied before the final report is made. There is a certain small percentage of error in the frozen section, but that is almost entirely a matter of experience.

The finding, years later, of another fibroadenoma or another cyst would not change our attitude, for we have found that a woman prefers to take the chance of another operation if she may keep her breast and be assured that in so doing she does not have any increased chance of malignancy developing in the breast.

While in saying that, we are aware that some surgeons adopt a different policy, and do an amputation of the breast especially for cystic and papillary conditions, because they consider them precancerous.

MALIGNANT TUMORS

These average about 59 per cent of the Roosevelt cases. They are people who have come to us, some, a few days, some, years after they first noticed the tumor. We have noticed that as a rule the private patients come earlier than the ward cases.

A large number of the cases are manifestly malignant, and in these cases it has been customary to do the radical operation without any attempt at quick section. This type is so familiar to all of you that a description of the clinical findings is needless. We feel that *x*-ray examination of the thorax and the bones is advisable in these advanced cases. If metastases are found, we usually see no advantage in any surgical treatment, and suggest either radium or *x*-rays.

When there is a question, however, we maintain that it is justifiable to make a curved incision at the lower border of the breast, make a wide excision of the tumor, and then, away from the operating table, make a gross and a microscopic examination. This may all be done in a few minutes and then the operation may be continued as indicated.

Many times the patient has thus been saved from a mutilating operation. For I care not who the clinician is, I defy him to tell accurately before operation, in many cases, whether the tumor is malignant or benign. We are told that we have increased the probable mortality because we have disturbed the solid lymph channels (of Hanley) away from the tumor by this procedure, and that the cancer cells have been let loose into the blood stream and done damage beyond repair. We feel that this is a theory that may have some germ of truth, but that it is greatly exaggerated. We do know this: that our late results are as good as those reported at other clinics where this is not the procedure, and the complete mastectomy is always done. Also incidentally, in cases where there has been an interval between the excision of the tumor and the later complete radical, as occurred in 9 of our cases for one reason or another, there was not the malignant fulminating course that so many allege to have occurred. Therefore, until we are proved wrong we feel that a local excision in doubtful cases is a wise procedure.

At this examination of the gross excised tumor we may quickly gain an excellent knowledge of the pathological

condition. The section with a scalpel gives us much information. Those with a gritty feel are very suggestive of malignancy, and the absence of a capsule with prolongation into the surrounding tissue means carcinoma. The scirrous type above described is the easiest. The yellow spots of themselves do not mean more than masses of epithelial cells which might well be in a benign tumor. The comedo-like effect obtained by pressure on the cut section is from detritus in large breast glands which may be benign. Hemorrhage in the tumor mass is very suggestive of malignancy. The trauma of excision does not cause that. The soft tumors are the most difficult. As I become more experienced I grow more skeptical of the capsule about a tumor and do not allow a picture of fibrous tissue at the periphery to make me decide right away that a capsule encloses the whole tumor. For often careful gross examination in several sections of the tumor discloses some point where there is no capsule and where the growth extends into the surrounding tissue. If the tumor shells out, it is benign. Unfortunately I have fallen rather hard on some of these cases on the question of a fibrous capsule, and I do not jump too quickly at a conclusion. During the past year, I had it forced again to my attention by a mistake in the case of the mother of one of the well-known pathologists in town—just the very man for whom we wanted to do well. In this instance we had to have the lady return for a radical procedure.

Tuberculosis with breast sinuses may be confused with an ulcerative carcinoma. Last year (1922) we had such a case treated by radical operation, and this proved to be tuberculosis. But there was no mishap, and it is a justifiable error. Incidentally, in 1915 we had one carcinoma of the breast with metastases to the axillary lymph-nodes, and these nodes showed tuberculosis. The patient returned the other day and some local recurrences were removed. There was no evidence of the tuberculosis.

Sarcoma is rare, and is apt to be confused with an edematous adenofibroma. Grossly the finding of glandular tissue in the histological section will help to exclude sarcoma. Occasionally, in a low-grade pyogenic mastitis which is well localized, the diagnosis cannot be made until the frozen

section is made, when an inflammatory process only is disclosed.

There is no reason to deny that the breast tumor is malignant because the patient is under twenty-five years. We see carcinoma often enough in other places in the young to know that the age of twenty-five is no lower limit to carcinoma. We think Dr. Bloodgood is unfortunate in stressing that point.

OPERATION

We believe that in carcinoma a radical operation is indicated. We advocate the transverse ovoid or the oblique ovoid incision. I know that in the hands of the men who use it, just as good a cleaning-out of the apex of the axilla is obtained in the transverse, as in the oblique ovoid in the hands of other men. And the Stewart incision has the advantage that it leaves a low scar, which allows the wearing of low-cut dresses.

The pectoralis major, with the exception of the clavicular portion, is removed. The pectoralis minor, except for its sheaths, is left *in situ*. A thorough dissection of the axilla is performed. A stab drain is made into the axilla, and the drain removed in forty-eight hours. We have not made the excision of the rectus abdominis as a routine. In the tumors of the lower hemisphere it has been generally used, but now I advise its practice as a routine procedure. In removing the skin a rather wide excision is made, and there is an oblique dissection of the fat well out from the skin incision, in order to include the dangerous lymphatics. Rarely do we take so much that the skin edges cannot be approximated. We think that such a procedure is usually unnecessary. The same may be said of the supraclavicular lymph-node excision at the same operation. When the metastases have reached there the operation is of little avail anyway. After operation, the forearm is bound to the chest until the patient is conscious, when it is allowed to be carried in a sling. Early movement, especially abduction, is indicated, and the patient is encouraged to touch the back of the neck and the lumbar region frequently during the day. If this is followed one may regularly expect good function of the arm at the shoulder joint.

1922

Benign tumors. 31
Galactocele. 1
Simple cysts. 3
Generalized cystic. 11

4 complete mastectomies, of which 1 was a radical (Russell) and another had had a partial mastectomy 6 years before

7 partial mastectomies

Papillary cyst adenomas. 2

One radical anteop. diagnosis cancer no local excision

One mastectomy no local excision

Chronic mastitis—radical mastectomy, orange-peel fixity, etc., no local, excision as preliminary

Tuberculosis—complete mastectomy—preoperative diagnosis cancer

Lipomas. 1
Phantom tumors. . . . . 1 (Reese Peck)
Adenofibromas. 10

8 had local excision

2 had mastectomy

Cancers 29 new cases

18 with axillary metastases, interval 14 months, shortest 4 days, longest 10 years

11 without axillary metastases, interval 6.6 months

16 out of the 29 had free skin

21 out of the 29 moved on the deep tissue

24 out of the 29 had a normal nipple

4 with metastases had no palpable axillary lymph-nodes

3 out of the 29 had two breast nodules to be felt

None had any nipple discharge

All had a radical except 1

One patient had had the other breast removed 8 years previously for cancer of the breast with axillary metastases.

X-RAYS

Without *x*-rays or radium we have been able to show five-year cures in 65 per cent of our non-metastatic cases, and 23 per cent cures in the cases that had axillary metastases. Since such is the result, we do not see how surgery can be abandoned in the favorable case. I think that most of the *x*-ray men agree that surgery is indicated in the treatment of cancer of the breast. Our point of difference is the question of *x*-rays or radium before operation.

Our surgical attitude has been: immediate operation followed by *x*-rays or radium. Our friends suggest that there

should be a preliminary course of *x*-rays when the diagnosis of cancer is made, then a wait of a month or six weeks before operation to allow the full effect of the radiation, then the operation, with the subsequent *x*-ray treatment indefinitely.

The *x*-ray has not yet cured a case of cancer, but surgery has given seventeen-year cures. Therefore, to me the obvious thing is to seize immediately the remedy that has had such good results. Then, by all means, after the patient has recovered from the effects of the operative procedure, give her *x*-ray treatment as best indicated, either in massive high voltage, with the subsequent temporary prostration, fever and depression, or the frequent moderated doses to ambulatory cases with less-marked depression. I am not possessed of the physical knowledge to say which is better. I do know that at times the massive high-voltage treatment has a more depressing effect and is more of a physical strain than the operative procedure. I am opposed to this massive treatment as a preliminary to operation. In the first place, with the general systemic it is a poor preparation to an extensive surgical procedure. Secondly, several cases in which I have studied the tumor after such a procedure have shown cancer cells which histologically looked alive and active, as judged by the appearance of the cell and the staining reaction. It is also fair to state that this same study showed cells that had degenerated and cells that were necrotic. Hence we believe that all the cells in the tumor are not killed by the *x*-ray. Perhaps small lymph cords of cancer cells in the periphery have been killed.

Another factor may be best illustrated by the history of a lady who was sent to Dr. Peck. He was suspicious of cancer, but could not say positively. He advised immediate excision.

As is often the case, this lady shopped around, and of her own accord, and on the advice of an eminent pathologist in New York, decided to have the preliminary *x*-ray course. She returned to the hospital six weeks later for the operation. And there, with an exploratory, Dr. Peck found that the patient had a single tense blue cyst—just as tense as if there had been no *x*-ray treatment. We said earlier that

it is well-nigh impossible to tell some cancers in the earlier stages from benign tumors. If our friend had appreciated this he would have allowed the immediate operative procedure and thus have saved the woman needless worry and expense.

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